ANNALS OF INTERNAL MEDICINE

PUBLISHED MONTHLY BY

The American College of Physicians

OL. 39 (O.S., Vol. XLIV)	OCTOBER,	1953	NUMBER
	CONTEN	TS	Page
Aseptic Meningitis, a Disease on 854 Cases. CHARLES			tiologic Studies
Relationship of Adiposity to Modification by Dietary	Serum Cholesterol Means. WELDON J	and Lipoprotein Le	evels and Their 705
Management of Cerebral Vas	cular Accidents. J	. M. NIELSEN	717
The Treatment of Hemochro and W. R. ARROWSMITH	matosis by Massive	Venesection. W.	D. DAVIS, JR. 723
Intra-Articular Hydrocortison			
Gastroduodenal Hemorrhage: by Palpation and Inspect			
Rheumatism and Arthritis: R Years (Tenth Rheumat EDWARD W. BOLAND, Jo ENGLEMAN, WALLACE GO CHARLES RAGAN, MARIA J. SMYTH	tism Review). Pa DEPH J. BUNIM,	DARRELL C. CRAIN LL LOCKIE, MAX M. VARD F. ROSENBERG	D. ROBINSON, EPHRAIM P. MONTGOMERY.
Case Reports:			
Spontaneous Hemopneum and Streptodornase.	PHILIP N. JONES	rence to the Use of and Roy S. BIGHAR	f Streptokinase u, Jr 907
Acute Hepatitis Due to I	Brucellosis. H. Nu	SHAN and A. A. B.	AILEY 915
Sickle Cell Anemia Term GOLDIN, KARL C. KE	inating in Acute M	Iyeloblastic Leukem BEARD	ia. Albert G. 920
An Unusual Case of Mas PAUL N. G. YU, FR NYE, JR. and JOHN I	ANK W. LOVEJOY.	JR., HOWARD A. JO	OOS, ROBERT E.
Obstruction of the Superi ROBERT E. MITCHELL	ior and Inferior Ve	nae Cavae in the So	ame Individual.
Cardiac Aneurysm with Review of the Litera			
Editorial-The Rôle of the In			
Reviews			962
			THE RESIDENCE OF THE PARTY OF T

THORACIC SURGERY AND RELATED PATHOLOGY

THORACIC SURCERY and RELATED PATHOLOGY Professor of Surject

AF E. LINDSKOG, M.D., P.A.C.S. Stirpers; als Univ. School of Malkelmo
A. VERILI A. LIEBOW, M.D.
Pribology, Yells Univ. School of Medicine

TITH COSTRIBUTIONS BY

RAIPH D. ALLEY, M.D., Clinical Instructor in Surgery, Alberry Modi-

HILLAM P. BLOOMER, M.D., Instructor in Surgery, Yale University

Hilling Shatorum Shelton Conn. Aut. Che. Professor of Medi-

The past several years have produced such material advances to thoracic surgery and so many major contributions to the literature as to make desirable a review and coordination of present knowledge within the confines of a single volume.

The purpose of this new text is to provide an analysis, synthesis and compilation supported by a clinical experience gained from the management of approximately 3500 patients admitted to the thoracis section of an active surgical department.

The book atreases such basic considerations as anatomy, physiology and pathology; many operative procedures are described and illustrated, but the main emphasis has not been placed on minutiae of operative technic.

For authors systemically over the diagnosis and treatment of traufas, infections, congenital and developmental abnormalities benign and malignant neoplasms and functional disorders of that against area which includes the chest wall, pleura, tracheobronchial tree, lunga, pericardium, heart, great ressels, mediastinum, esophages and diaphrage.

Seven chapters detail the surgical trestment of tuberculors. A separate chapter is devoted to preoperative preparation, operative and postoperative care, and a concluding chapter deals with postoperative pulmonary complications.

The numerous illustrations include rountgenograms and photographs, diagrammatic sketches and half-tone drawings.

CHOP 15

PUBL. AUG. 1958. 686 PAGES.

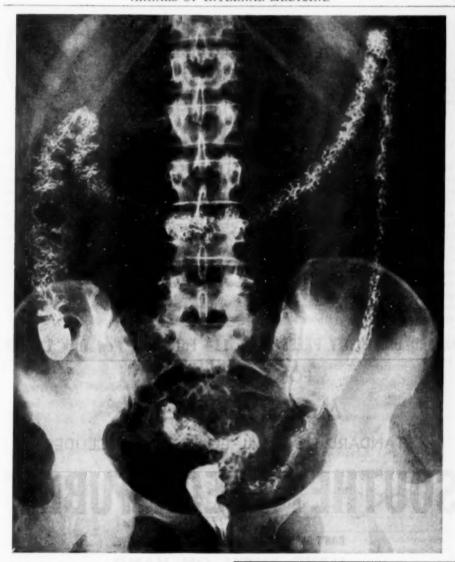
362 ILLUSTRATIONS.

815.00

APPLETON-CENTURY-CROFTS, INC.

35 W. 32nd Street, New York I, N. Y.

Subscription per annum, we possibild, \$10.00, United States, Causelle, Mexico, Cufes, Causal Zone, Hawail, Possibile, Philippine Islands, Central and South American Countries, and Spatin; \$11.00, other countries. Entered as Second Class Matter August 21, 1825, at the Post Office of Lincolnty, Pa., under the Act of March Intered as Second Class Matter August 21, 1825, at the Post Office of Lincolnty, Pa., under the Act of Pobruary 22, 1825, at 1820, accordance for mailing at a spacial rate of postage provided for in the Act of Pobruary 22, 1825, accordance for mailing at a spacial rate of 1846, P. L. & E. of 1848, authorised October 7, 1806,



VISCERAL RADIOLOGY

(Markovits)

Virtually a complete encyclopedia of radiological diagnostic procedure, the book correlates clinical aspects with radiological studies. It is invaluable to the internist as a reliable diagnostic workbook.

612 pp., 667 Illus.

\$24.00

BONE AND JOINT RADIOLOGY \$20.00

Now in preparation:

Hormones in Health & Disease

To: The Macmillan Company, Box C-3 60 Fifth Avenue, New York II, N.Y. Please send me:

- FREE—The NEW Medical Book Catalog. Viscaral Radiology and bill me for \$24.00 plus small delivery charge.

Name Address

City

Please Mention this Journal when writing to Advertisers

Coming Soon MEDICAL TREATMENT OF DISEASE

By the Late Henry A. Christian, M.D., Sc.D., M.A.C.P., D.S.M., Hersey Professor, Emeritus, of the Theory and Practice of Physic, Harvard University; Dale G. Friend, M.D., F.A.C.P., Associate in Medicine, Peter Bent Brigham Hospital, Boston, Massachusetts; Maurice A. Schnitker, B.S., M.D., F.A.C.P., Director of Medicine, St. Vincent's Hospital, Toledo, Ohio.



Volume 8 of the OXFORD LOOSE-LEAF MEDICINE to be Sold Separately

1953 1,015 pages

Cloth (Semi-Limp Loose Leaf Binding)

This volume describes medical treatment for all principal diseases to which medical treatment could or should be applied. It combines the loose-leaf idea with the selection of really proved methods of therapy in a loose-leaf binder only 7" x 85%" overall. It assumes that the diagnosis will already have been made and includes the recommended treatment, or treatments, where alternative treatments are indicated, including prophylaxis. Reliability proved by effectiveness in clinical use as shown from controlled observations of patients, is the keystone of the book. Although the purpose of its publication is to bring forward the newer treatments of proved reliability, no treatment is included for its novelty or even its promise. The loose-leaf format permits the addition of future new treatments, or their substitution for older ones to which they may be superior, as fast as successful clinical use recommends them. The drugs recommended have been carefully selected for their pharmacological action. Official drug terminology is used throughout, but common trade names are often given in parenthesis. Purchasers of this book, by application, may automatically receive future additional loose-leaf supplements to keep the volume current with the developments in therapeutics.

OXFORD UNIVERSITY PRESS, INC., 114 Fifth Ave., New York 11, N.Y.

FOR THE RELIEF OF

MASSIVE EDEMA

STANDARD HOSPITAL EQUIPMENT INCLUDES

SOUTHEY-LEECH TUBES*

DON'T WAIT UNTIL THE NEED IS IMPERATIVE.
HAVE THEM ON HAND

*Fiese, M. J., and Thayer, J. M.: Archives, Int. Med. 85:132 (Jan. 1950)

Prepare for that emergency—Clip Coupon Now Please send — sets of Southey-Leech Tubes, complete with trocar and drainage tubing at \$12.00 per set to:	4=	Tubes and treeze made of rust-resists alver-nickel. Will last indefinitely. Or a set to have on hand. Ask year loop to keep them on hand.							
Name:	760	Reigna	Company						
Street:	1100								
City:	82 WATERMAN ST. PROVIDENCE 6, RHODE ISLAND								



THE HEART BEAT

Graphic Methods in the Study of THE CARDIAC PATIENT

by ALDO A. LUISADA, M.D.

Prof. of Medicine & Director, Div. of Cardiology, The Chicago Medical School; Associate Visiting Phys. & Chief of Cardiac Clinics, Mt. Sinai Hosp. of Chicago.

HERE is an account of the available procedures for tracing cardiac motion, arterial and venous pulses, electrical manifestations of the heart, as well as for intrathoracic and intracardiac pressures. This information is correlated usefully for the first time since Sir Thomas Lewis' classic work, "The Mechanism and Graphic Registration of the Heart Beat" in 1924.

The text is illuminated by several hundred tracings obtained by modern technics and accurately reproduced. This outstanding monograph will be a valuable source book for all clinicians and investigators concerned with the heart, its disorders and function.

Be sure to examine a copy of this brand new book. Sent On Approval.

531 pp., 273 illus., \$12.00



A HOEBER-HARPER BOOK

RETURN THIS HANDY ORDER FORM NOW

PAU 49 New	E.	3	3		d		5	1	r	e					ı	N	10	C																			AI	nel	10	83
	eas															-																					•		•	_
Luis	ad:	a T	5		T	ľ	1	E		ŀ	1	E	A	V	R	T		ı	3	E	A	I	Γ			*						*		10		1	Z	.(U	U
			B	il	1	1	W	e															(1	R	:	C	E	n	C	le	Di	50	20	ł				
					((F	3	e	tu	ır	'n		P	ri	v	il	e	9	e	s,	,	0	f	c	0	u	r	50	•))										
Nam	e		*																		4						*	*								*		*		
Addr	ess						•						*	×			*	*	×	*	*	*		*		*						*	*		*					

TWO NEW 1953 BOOKS

Herbut—Gynecological and Obstetrical Pathology

By PETER A. HERBUT, M.D.

Professor of Pathology, Jefferson Medical College and Director of Clinical Laboratories, Jefferson Medical College Hospital, Philadelphia, Pa.

Diagnosis and treatment! Pathological lesions of the female generative tract are described systematically and in detail in this sound clinical work. It will prove especially useful to internists, pathologists, gynecologists and obstetricians, and furnishes long-needed guidance to practitioners who usually see these conditions first. Diseases are presented from a regional point of view with the vulva, vagina, uterine cervix, uterus, fallopian tubes, ovaries and placenta discussed fully in separate chapters. The text is exceptionally well illustrated throughout.

New. 683 Pages. 428 Illustrations on 246 Figures and 2 Plates in Color. \$12.50

Epstein and Davidoff— An Atlas of Skull Roentgenograms

By BERNARD S. EPSTEIN, M.D.

Associate Radiologist, The Jewish Hospital
of Brooklyn, N. Y.

and LEO M. DAVIDOFF, M.D.

Neurosurgeon, Mount Sinal Hospital, New York;
Director of Neurological Surgery,
The Beth Israel Hospital,
New York

This book contains an outstanding collection of unretouched roentgenograms, reproduced in as large a format as possible, to permit excellent visualizations of lesions of the skull. Differential diagnostic hints are worked expertly into the text and into the legends which accompany the more than 600 illustrations. Similarities and differences are emphasized.

New. 415 Pages, 7" × 10". 603 Illustrations on 315 Figures. \$15.00

Washington Square LEA & FEBIGER Philadelphia 6, Pa.

1953 DIRECTORY

American College of Physicians

The newly revised and enlarged Directory of the American College of Physicians, now at press, will be ready shortly for delivery. Members who placed pre-publication orders will receive their copies in the first mailing. Life Fellows will receive copies free.

Every member of the College, most medical institutions and others needing reference sources of this character should have this Directory at hand.

- Current and Past ACP Data
- Constitution & By-Laws
- Biographical Data Re Members
- Sturdy Cloth Binding; Approximately 1,000 pages

\$6.00 per copy, postpaid

Limited Supply

American College of Physicians 4200 Pine St., Philadelphia 4, Pa.

WANTED

Back Issues of

ANNALS OF INTERNAL MEDICINE

Good used copies of the following issues are now needed. Only those issues which are currently being advertised will be accepted.

\$1.50 each for

Vol. I, No. 1—July, 1927
Vol. I, No. 2—August, 1927
Vol. I, No. 4—October, 1927
Vol. II, No. 4—October, 1927
Vol. II, No. 3—September, 1929
Vol. I, No. 3—September, 1927
Vol. I, No. 4—December, 1927
Vol. I, No. 4—December, 1927
Vol. I, No. 5—March, 1928
Vol. I, No. 8—February, 1928
Vol. I, No. 1—July, 1928
Vol. II, No. 1—July, 1928
Vol. II, No. 1—July, 1932
Vol. VI, No. 1—July, 1932
Vol. VI, No. 4—October, 1832

76f each for ol. XXXVIII, No. 1—January, 1953 ol. XXXVIII, No. 2—February, 1963 ol. XXXVIII, No. 4—April, 1963

Address Journals to:

E. R. LOVELAND, Executive Secretary
4200 Pine Street Philadelphia 4, Pa.

Please Mention this Journal when writing to Advertisers

NEW BOOKS FROM WILLIAMS & WILKINS

WATER, ELECTROLYTE AND ACID-BASE BALANCE

Normal and Pathologic Physiology as a Basis for Therapy

By HARRY F. WEISBERG, M.D.

Covers the entire subject in a comprehensive and practical manner.

Integrates basic concepts with current developments. Correlates the essential physiologic and chemical facts, and applies them to clinical medicine.

Emphasizes the fact that the therapy of each patient is a separate problem. Gives you a thorough understanding of the normal and pathologic physiology to use as a basis for individualized therapy.

Guides you in planning your program of therapy and in keeping it flexible—not only from one case to another but from one day to another in the same case.

Includes well-planned tables and figures that will serve you as a rapid summary; extensive list of references, glossary, index.

250 pp., 10 figs., 29 tables, \$5.00

DIURETIC THERAPY

The Pharmacology of Diuretic Agents and the Clinical Management of the Edematous Patient

By ALPRED VOGL. M.D.

Assembles all the pertinent material and supplies you with a comprehensive and accurate knowledge of the subject.

Shows you how to individualize diuretic therapy by adapting it to the particular needs and responses of the patient, and how to restore many a patient in an unresponsive and apparently hopeless condition to a reasonable state of health and comfort.

Presents clear discussions of the pathogenesis of the different types of edema, and of the action of the various drugs and therapeutic procedures which you can use to formulate a rational and effective plan of treatment in each case.

250 pp., 5 figs., \$5.00

CLINICAL CARDIOLOGY

Edited by Franklin C. Massey, With 33 Able Collaborators.

A new and refreshing approach to a subject of wide and timely interest.

Forms a composite picture representing the heart and its function in regard to the total organism.

Features sections on many allied specialties: pediatrics, metabolism, surgery, anesthesiology, obstetrics, endocrinology, psychiatry, etc.

Covers physical diagnosis, roentgenology, electrocardiography, congenital heart disease, infections, the major bases for the several kinds of heart disease, special types of cardiac involvement, etc.

Includes free expressions of opinion on many controversial matters.

1116 pp., 208 figs., \$13.50

THE WILLIAMS & WILKINS COMPANY Mt. Royal and Guilford Aves. Baltimore 2, Maryland

a new advance in the control of tuberculosis

Drug therapy for the management of tuberculosis continues to advance at a rapid pace. In keeping with the latest improvement—which promises a substantially lower incidence of vestibular and auditory toxicity—Pfizer has made available a new combination of streptomycin and dihydrostreptomycin—

Combistrep*



Available in vials of 1 Gm. and 5 Gm., dry powder for preparation of solutions for intramuscular injection.

also

Recent clinical studies¹ have shown that such a combination, one-half streptomycin and one-half dihydrostreptomycin, gave rise to a significant reduction in neurotoxic side effects as compared to equivalent dosage of either drug used alone, even though administered over the prolonged treatment periods required for the control of tuberculosis.

Combistrep offers these benefits to the tuberculous patient with the further assurance that its purity is of the same high standard typical of all Pfizer pharmaceuticals.

 Heck, W. E.: Reduced Ototoxicity by Combined Streptomycin-Dihydrostreptomycin Treatment of Tuberculosis, Scientific Exhibit 317, 102nd Annual Meeting A.M.A., New York, June 1-5, 1953.

Streptomycin Sulfate - dry powder and solution

Dihydrostreptomycin Sulfate - dry powder and solution

Streptohydrazid*—a crystalline compound combining streptomycin and isoniazid

Cotinazin®—brand of isoniazid

Viocin* Sulfate—brand of viomycin, for resistant cases of tuberculosis

Pfizer Laboratories, DIVISION, CHAS. PFIZER & CO., INC., BROOKLYN 6, N.Y.

-

Please Mention this Journal when writing to Advertisers





ERATRUM ALBUM, a species of Veratrum indigenous

to southern Europe, yields the ester alkaloid 'Provell Maleate.' 'Provell Maleate' is many times more potent than the mixture of substances from which it is isolated. Its uniformity and purity permit better control of the hypertensive patient than is possible with mixtures of alkaloids.

Hoobler* states that protoveratrine is superior to the alkaloids from Veratrum viride in that blood pressure can be reduced from six to eight hours daily without producing nausea, vomiting, or tolerance to the medication. The purity of the alkaloid allows for the accurate dosage so necessary to continuing good results over extended periods of time. Careful adjustment of the dosage schedule to fit the need of each patient is mandatory. Overdosage may result in distressing, although usually not serious, symptoms. 'Provell Maleate' is a potent drug to be administered only under the close supervision of a physician.

'Provell Maleate,' 0.5 mg., is available in cross-scored tablets (to facilitate careful individualization of dosage) in bottles of 100. Your pharmacist has it. Be sure to evaluate carefully this important hypotensive drug. Ask the Lilly representative ... or write Eli Lilly and Company, Indianapolis 6, Indiana, U. S. A., for more complete pharmacologic and clinical data.

*Annals of Internal Medicine, 37:465, 1952.

PROVELL MALEATE

(PROTOVERATRINE A AND B MALEATES, LILLY)



consistently, safely



for your peptic ulcer patients...

Antrenyl

bromide

OKEPHENONIUM BOUNDE CIBA

New High Potency Anticholinergic with No Bitter Aftertaste

As adjunctive therapy in your standard peptic ulcer regimen*, Antrenyl offers potent anticholinergic action to inhibit motility of the gastrointestinal tract and gastric secretion.

Although Antrenyl is one of the most potent of all anticholinergic agents, it rarely causes esophageal or gastric irritation and has no bitter aftertaste. In individualized doses, it is well tolerated and side effects are absent or generally mild.

In one study¹ patients receiving Antrenyl obtained relief from acute symptoms within 24 to 36 hours. Dosage was individually adjusted at 5 to 10 mg. four times a day. Side effects were adjudged less pronounced than those of other similar agents ordinarily used in the management of peptic ulcer.

Prescribe Antrenyl in your next case of peptic ulcer and spasm of the gastrointestinal tract. Available as tablets, 5 mg., scored, bottles of 100; and syrup, 5 mg. per teaspoonful (4 cc.), bottles of 1 pint.

Ciba Pharmaceutical Products, Inc., Summit, N. J.

Leading gastroenterologists recommend:

rest sedation antacids nonirritating diet anticholinergies

Cillban

1. Rogers, M. P., and Gray, C. L.: Am. J. Digest. Dis. 19:180, 1952.

1/ 1895M

A new useful combination -

...for antibacterial therapy:

GANTRICILLIN 300 'Roche.'

Each tablet provides 300,000

units of penicillin PLUS 0.5 Gm

of Gantrisin, the highly soluble,

wide-spectrum single sulfonamide.

Gantricillin-300
- a new
antibacterial -

For wide-spectrum, oral antibacterial therapy -- Gantricillin -300 'Roche'-Gantrisin plus penicillin in a single tablet.



Invitation to asthma?

not necessarily...

Tedral, taken at the first sign of attack, often forestalls severe symptoms.

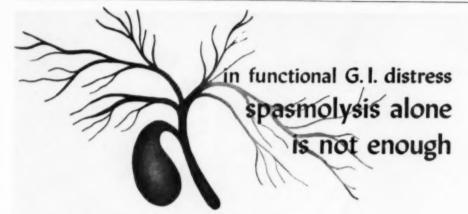
relief in minutes... Tedral brings symptomatic relief in a matter of minutes. Breathing becomes easier as Tedral relaxes smooth muscle, reduces tissue edema, provides mild sedation.

for 4 full hours... Tedral maintains more normal respiration for a sustained period—not just a momentary pause in the attack. **Prompt and prolonged relief** with Tedral can be initiated any time, day or night, whenever needed, without fear of incapacitating side effects.

Tedral provides:
theophylline 2 gr.
ephedrine 3/8 gr.
phenobarbital 4/8 gr.
in boxes of 24, 120 and 1000 tablets

Tedral

WARNER-CHILCOTT



For prompt and more effective relief of belching, bloating, flatulence, nausea, indigestion and constipation, prescribe *Decholin/Belladonna* for

reliable spasmolysis

- · inhibits smooth-muscle spasm
- · suppresses incoordinate peristalsis
- · facilitates biliary and pancreatic drainage

improved liver function

- · increases bile flow and fluidity through hydrocholeresis
- · enhances blood supply to liver
- · provides mild, natural laxation without catharsis

DECHOLIN® with BELLADONNA

Dosage: One or, if necessary, two Decholin/Belladonna Tablets three times daily.

Composition: Each tablet of Decholin/Belladonna contains Decholin (dehydrocholic acid, AMES) 3% gr., and ext. of belladonna, 1/6 gr. (equivalent to tincture of belladonna, 7 minims). Bottles of 100.

AMES COMPANY, INC

ELKHART, INDIANA Ames Company of Canada, Ltd., Toronto

.....

CLINICAL EVALUATION FREQUENTLY FAVORS BUTAZOLIDIN®

In antiarthritic potency, BUTAZOLIDIN can be compared only with gold, ACTH and cortisone. In making a choice between these agents, the specific advantages of BUTAZOLIDIN merit consideration:

- Simple oral administration
- ■Potent and prompt antiarthritic effect
- ■Broad spectrum of action embracing many forms of arthritis
- ■No development of tolerance requiring progressively increasing dosage
 - ■No disturbance of normal hormonal balance
 - Moderate in cost

As with any agent so potent as BUTAZOLIDIN, optimal therapeutic results with minimal risk of side reactions can only be obtained by clinical management based on careful selection of patients, proper regulation of dosage, and regular observation of each patient.

Detailed Literature on Request.

BUTAZOLIDIN® (brand of phenylbutazone) Tablets of 100 mg.

GEIGY PHARMACEUTICALS



Division of Geigy Company, Inc. 220 Church Street, New York 13, N.Y. In Canada: Geigy (Canada) Limited, Montreal



IN ARTHRITIS

To obtain maximum results, high salicylate blood levels are required. This means high oral dosage which can be attained, without excessive gastric disturbance, by using Salcedrox.

three jumps ahead.

Salcedrox virtually eliminates gastric disturbance, because of the protective combination with activated aluminum hydroxide and calcium carbonate.

Salcedrox also contains a high dose of vitamin C, because it has been observed that rheumatic and arthritic states show vitamin C deficiencies, and salicylate therapy has a tendency to intensify depletion of vitamin C.

There is significant evidence that salicylates, through action on the hypothalamus, stimulate the pituitary, producing an ACTH-like effect on the adrenal cortex.*

This new concept of salicylate action explains many of the clinical results obtained with salicylate therapy in the treatment of arthritides and rheumatic afflictions—observed results that cannot be attributed to analgesic action alone.

*Proceedings Soc. Exp. Dio. Med., 1952, v80, 51-55, G. Cronheim, et al.

Sedium Salicylate 5 gr. (0.3 Gm.)

Atuminum Hydroxide Gel.

dried ... 2 gr. (0.12 Gm.)

dried 2 gr. (0.12 Gm.)
Catcium Ascorbote ... 1 gr. (60 mg.)
(equivalent to 50 mg. Ascorbic
Acid)

Catcium Carbonato 1 gr. (60 mg.)

massive salicylate dosage

> high blood levels

maximum gastric tolerance

massengill

BRISTOL, TENN.

send for professional literature **SALCEDROX**

DR. WILLIAM B. TERHUNE and THE SILVER HILL FOUNDATION

Announce:

APPOINTMENTS AVAILABLE FOR RESIDENTS AND ASSOCIATES IN THE TRAINING AND ACTIVE PRACTICE OF PSYCHOSOMATIC MEDICINE AS APPLIED SPECIFICALLY TO THE TREATMENT OF THE PSYCHONEUROSES.

Generous compensation and opportunity for permanent staff appointment.

The Silver Hill Foundation is a psychotherapeutic unit for the treatment of the functional nervous disorders (the psychoneuroses, psychosomatic disturbances and social psychiatric disorders). The setting is that of a comfortable country home devoid of sanatorium atmosphere where a limited number of patients are under intensive, re-educational treatment for a period of several weeks.

Only applicants with excellent educational background will be considered.

APPLY TO: Dr. William B. Terhune, F.A.C.P., Medical Director, New Canaan, Connecticut

Associates: DR. FRANKLIN S. DuBOIS, F.A.C.P., DR. ROBERT B. HIDEN, F.A.C.P., DR. MARVIN G. PEARCE, DR. JOHN A. ATCHLEY, DR. WILSON G. SCANLON, DR. HARDIN M. RITCHEY

In spastic and occlusive vascular diseases



Tensodin Tablets 100's, 500's and 1000's

Tennodin®, a product of E. Bilhuber, Inc.

TENSODIN

Tensodin is indicated in angina pectoris and other coronary and peripheral vascular conditions for its antispasmodic, vasodilator and sedative effects. The usual dose is one or two tablets every four hours.

No narcotic prescription is required.

Each Tensodin tablet contains ethaverine hydrochloride (non-narcotic ethyl homolog of papaverine) ½ grain, phenobarbital ¼ grain and theophylline calcium salicylate 3 grains.

BILHUBER-KNOLL CORP. distributor

ORANGE NEW JERSEY



\$15.00 each (postage extra) \$20.00 each \$35.00 pair HARVEY IMHOTEP (postage extra) PASTEUR HIPPOCRATES ROENTGEN GALEN ☐ IMHOTEP LISTER MAIMONIDES ROENTGEN HIPPOCRATES PASTEUR VESALIUS OSLER OSLER. ☐ MAIMONIDES Illustrated descriptive folder sent on request. Can be ordered direct from studio or from: Distributors: Brown and Connolly, Boston, Mass. Chicago Medical Book Company, Chicago, III. George Eliot Medical and Scientific Books, New York, N. Y. To be sent to Matthews Medical Books, St. Louis, Mo. J. A. Majors Check Enclosed Company, Dallas, Texas; Atlanta, Ga.; New Orleans, ☐ Charge If ordered as gift, please enclose personal card. La. Rittenhouse Book Store, Philadelphia, Pa. DORIS APPEL MEDICAL SCULPTURES STUDIO: 281 Ocean St., Lynn, Mass.

PLAQUES

BOOKEND STATUES

for peptic ulcer...

only

PRANTAL

offers all four

- 1 rapid relief from pain and other ulcer symptoms
- 2 accelerated healing
- 3 outstanding freedom from side effects
- 4 dosage forms that individualize therapy:



PRANTAL Injection for acute episodes.

PRANTAL Tablets (plainscored), for adjusting therapy. PRANTAL Repeat Action Tablets, (coated—no taste) —for prolonged effect— (8 hours or more).

and !

PRANTAL

Tablets with Phenobarbital 16 mg. (coated—no taste)—for combined sedative and anticholinergic effects.

Praytage methylasilate (board of diphonoschaull makylauliste).



CHERING CORPORATION . BLOOMFIELD, NEW JERSE



ANDROGENS

when

endocrine

therapy

is a key

to well-being

Specify



ESTROGENS



PROGESTERONES



COMBINATIONS



SPECIALTY

SYNANDROTABS*	Methyl Testosterone, U.S.P., Tablets 10 mg. and 25 mg.
SYNANDRETS*	Testosterone, U.S.P., Transmucosal Tablets 10 mg. and 25 mg.
SYNANDROL*	Testosterone Propionate, U.S.P., in Sesame Oil 25 mg., 50 mg. and 100 mg. per cc.; in single-dose disposable STERAJECT® cartridges and in 10 cc. multiple-dose vials
SYNANDROL*-F	Testosterone, U.S.P., in Aqueous Suspension 25 mg., 50 mg. and 100 mg. per cc.; in 10 cc. multiple-dose vials
DIOGYNETS*	Estradiol, U.S.P., Transmucosal Tablets 0.125 mg., 0.25 mg. and 1.0 mg.
DIOGYN'-E	Ethinyl Estradiol Tablets 0.02 mg., 0.05 mg. and 0.5 mg.
DIOGYN*	Estradiol, U.S.P., in Aqueous Suspension 0.25 mg. and 1.0 mg. per cc.; in single-dose disposable STERAJECT cartridges and in 10 cc. multiple-dose vials
DIOGYN'-B	Estradiol Benzoate, U.S.P., in Sesame Oil 0.33 mg. and 1.0 mg. per cc.; in 10 cc. multiple-dose vials
ESTRONE	Estrone, U.S.P., in Aqueous Suspension 2 mg. and 5 mg. per cc.; in 10 cc. multiple-dose vials
SYNGESTROTABS*	Ethisterone, U.S.P., Tablets 10 mg., 25 mg. and 50 mg.
SYNGESTRETS*	Progesterone, U.S.P., Transmucosal Tablets 10 mg., 20 mg. and 50 mg.
SYNGESTERONE* IN SESAME OIL	Progesterone, U.S.P., in Sesame Oil 10 mg., 25 mg., 50 mg. and 100 mg. per cc.; in single-dose disposable STERAJECT cartridges and in 10 cc. multiple-dose vials
SYNGESTERONE* IN AQUEOUS SUSPENSION	Progesterone, U.S.P., in Aqueous Suspension 25 mg. and 50 mg. per cc.; in 10 cc. multiple-dose vials
COMBANDRIN*	Estradiol Benzoate, U.S.P., 1 mg. per ec. and Testosterone Pro- pionate, U.S.P. 20 mg. per cc. in Sesame Oil. In single-dose disposable STERAJECT cartridges and in 10 cc. multiple- dose vials
COMBANDRETS*	Estradiol, U.S.P., 1 mg. and Testosterone, U.S.P., 10 mg. per Transmucosal Tablet
NEODROL*	Stanolone in Aqueous Suspension 50 mg. per cc.; in 10 cc. multiple-dose vials *TRADEMARK Pfizer Syntex Products
PFIZER LABORATORIES	Division, Chas. Pfizer & Co., Inc. Brooklyn 6, N. Y.



AMPHOJEL®

ALUMINUM HYDROXIDE GEL WYETH'S ALUMINA GEL

In uncomplicated
PEPTIC ULCER
prompt healing may
be anticipated when
acid and pepsin
corrosion are halted.
"Double-Gel action" of
Amphojel provides
both local physical
protection and gentle
sustained antacid effect.







for caloric boost without gastric burden ...when weight gain is the objective

EDIOL

[ORAL FAT EMULSION SCHENLEY]

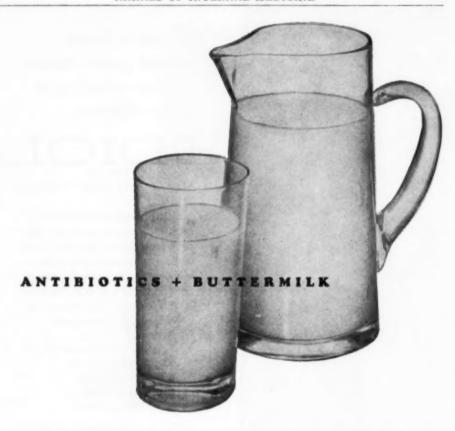
Just 2 tablespoonfuls of EDIOL* oral fat emulsion q.i.d. add 600 extra calories to the daily diet without increasing bulk intake or blunting the appetite for essential foods. This EDIOL regimen is the caloric equivalent of:

6 servings of macaroni and cheese, or 1 dozen Parker House rolls, or 12 pats of butter, or 8 boiled eggs, or 6 baked potatoes, or 91/2 slices of bread

EDIOL is an exceptionally palatable, creamy emulsion of vegetable oil (50%) and sucrose (12½%). The unusually fine particle size of EDIOL (average, I micron) favors ease of digestion, rapid assimilation. For children, or when fat tolerance is a problem, small initial dosage may be prescribed, then increased to the level of individual tolerance. Available through all pharmacies, in bottles of 16 fl.oz.

schenley

SCHENLEY LABORATORIES, INC.
LAWRENCEBURG, INDIANA



today, more and more clinicians are finding buttermilk useful in counteracting the undesirable
intestinal side effects frequently associated with
the administration of antibiotics¹ • when antibiotics or chemotherapy adversely influence the
normal intestinal flora, restoration of a healthy
bacterial balance is important • current medical
studies and reports from many doctors indicate
marked therapeutic benefit is obtained from both
the simultaneous and subsequent administration
of buttermilk² • even in cases of serious anorectal complications¹ • WHY BUTTERMILK²
• because it is an excellent source of "friendly
flora" that promote good digestion and elimination • because buttermilk also contributes to the

general health of the patient • it provides all the nutrients of whole milk with the exception of fat — here is a therapeutic food readily available, easily tolerated, pleasant tasting and low in cost • WHY BORDEN'S BUTTERMILK? • because it is made by exacting standards, from the careful choice of "starter" right down to the final check of critical culturing time • the same quality controls are applied to it that are used in the processing of highly perishable fresh milk • BORDEN'S BUTTERMILK is uniform, and pleasant tasting — not overly acid • it's truly buttermilk at its best.

 Manheim, S. D.: New York State J. Med. 51/2759 (Dec.) 1951.

2. Tice, L. P.: Philadelphia Med. 45:1135 (Mar. 25) 1950.

Manufacturers and distributors of BORDEN'S Instant Coffee STARLAC non-fat dry milk * BORDEN'S Evaporated Milk Fresh Milk * Ice Cream * Cheese BREMIL powdered infant food * MULL-SOY hypoallergenic food BIOLAC infant food * DRYCO infant food * KLIM powdered whole milk

The Borden Company
350 Madison Avenue, New York 17, N. Y.

LaMOTTE BLOOD CHEMISTRY OUTFITS

A complete line of approved Blood Chemistry Outfits, simplified so as to render accurate results with minimum time and operation.

Units available for

Albumin and Sugar in Urine
Alcohol in Blood and Urine
Alveolar Air CO₂ Tension
Bilirubin in Blood
Blood Losa in Blood
Fluids
Bromides in Blood
Calcium-Phosphorus in Blood
Calcium-Phosphorus in Blood
Creatinine in Blood
Cholesterol in Blood
Creatinine in Blood
Gastric Acidity
Hemoglobinometer
Icterus Index (Pigford)
Icterus Index (Micro)
Kline Test for Syphilis

Information on above cheerfully furnished.

If you do not have The LaMotte Blood Chemistry Handbook, a complimentary copy will be sent upon request.

LaMotte Chemical Products Co.

Dept. "C"

Towson, Baltimore 4, Md.

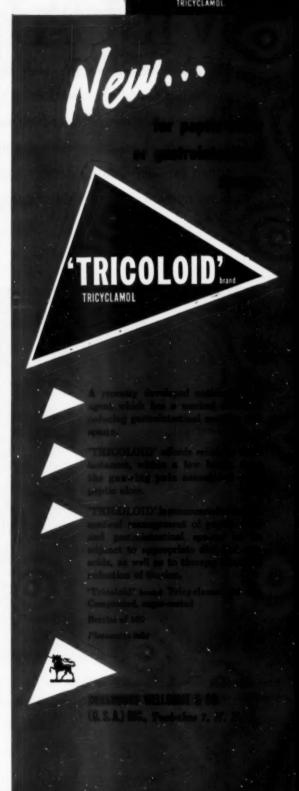
ANNALS VOLUME FILES

Before you decide to bind your Annals of Internal Medicine, consider the Jesse Jones Volume File. It holds an entire volume; each of the six issues is readily accessible.

- ATTRACTIVE—Red and green Kivar cover with gold-leaf lettering makes it a fit companion for your finest bindings.
- STURDY—Will support 150 pounds; no danger of its being crushed by heavy books.
- EXCLUSIVE—Especially designed and produced for the Annals, and is available only from the College.
- ECONOMICAL—Sent postpaid, carefully packed, for \$2.50 each, 3 for \$7.00, or 6 for \$13.00.

AMERICAN COLLEGE OF PHYSICIANS

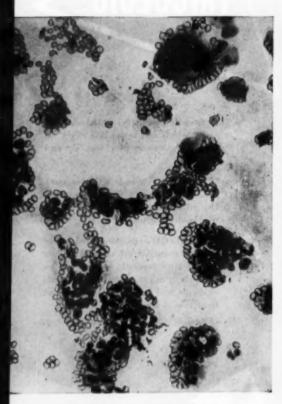
4200 Pine St., Philadelphia 4, Pa.



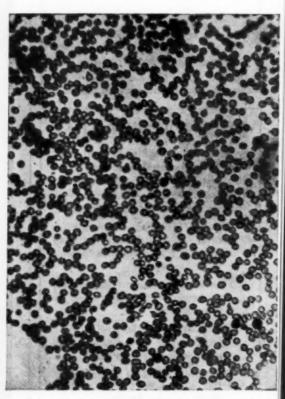
VISUAL PROOF

The photomicrographs illustrate the action of therapeutic level cobalt in producing actual regeneration of erythrocytes and their precursors even in severely depressed human bone marrow.¹

Because of extensive clinical studies with RONCOVITE—the original cobalt product—this understanding of direct stimulation of the depressed bone marrow has brought a completely new approach to the treatment of "secondary" anemia.



Bone marrow showing—acquired erythrocytic hypoplasia—no nucleated erythrocytes.



Same patient showing—active erythropoiesis following cobalt therapy.

of the Unique Hematologic Action of Therapeutic Cobalt

In Anemia Accompanying Infection—Roncovite

—provides such a significant advance in treatment of this usually refractory condition—acts so dramatically—that in severe cases it may make transfusion unnecessary.²

In Prolonged "Low-Grade" Anemias—

—where the response to iron is often relatively slow and unsatisfactory—Roncovite produces a 4-fold increase in erythrocyte production and an accelerated rate of hemoglobin synthesis.³ In these cases Roncovite overcomes the erythropoietic inhibition which has blocked improvement in the blood picture.

Roncovite provides successful therapy in the great majority of *all* the microcytic and normocytic anemias commonly seen in practice. (Roncovite is of the same low order of toxicity as iron.)

Subjective Improvement As Well-

Improvement is often rapid, with the patient voluntarily reporting an increased sense of well being within a few days. Such results have been documented and repeatedly confirmed in clinical use.

Suggested Dosage: One tablet four times daily in adults; 0.6 cc. daily in infants.

RONCOVITE

Dosage Forms

Roncovite Tabletz—enteric coated, red, each contains cobalt chloride, 15 mg.; ferrous sulfate, 0.2 Gm.; bottles of 100.

Roncovite Drops—each 0.6 cc. contains cobalt chloride, 40 mg.; ferrous sulfate, 75 mg.; bottles of 15 cc. with calibrated dropper.

-Write for literature and complete bibliography.

LLOYD BROTHERS, INC.

CINCINNATI 3, OHIO

In the Interest of Medicine Since 1870

- 1. Case 2, Seaman, A. J., and Koler, R.; Acta Hematologica, 9:153, 1953.
- Gardner, Frank H., J. Lab. Clin. Med.; 41:56, 1953.
- 3, Rohn, R. J. and Band, Wm. H., J. Lancet, 73:301, 1953.



"This is what I call SERVICE!"

This Viso-Cardiette technician is reading her latest copy of the bi-monthly Sanborn Technical Bulletin, popular publication which is a continuous and free-of-charge part of our Service-to-Owners picture.

In each issue she finds helpful hints and reminders on Viso (and Metabulator) maintenance and operating procedure, trouble-shooting articles, ideas and techniques developed by other technicians, information on accessories, and the like — all prepared and edited by an experienced staff for the sole purpose of helping her do a better job.

The doctor, too, finds much of interest in the Bulletin — such as results of Bulletin surveys to determine the most commonly used leads and which data spaces are most wanted on mounting cards, notices of postgraduate courses and textbooks, nomenclature and derivation of present-day leads, news of new equipment, and many clinically helpful articles.

And, the framed certificate proudly displayed in the scene above indicates that this technician has also seen her name in the Bulletin as a "graduate" of the Sanborn Electrocardiograph Service Course which she chose to take, by correspondence and at a nominal cost, for the information and understanding in operating technique it provides beyond the carefully-prepared Instruction Manual.

These EXCLUSIVE Service Helps are available ONLY to users of SANBORN electrocardiographs and metabolism testers. And both the Bulletin and the Service Course are only part of the many benefits received by Sanborn owners.

SANBORN

COMPANY



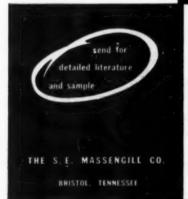
Aminodrox

Aminodrox

Heard at the staff meeting . . .



Aminodrox increases the usefulness of oral aminophylline



In the form of AMINODROX, three out of four patients can be given therapeutically effective oral doses of aminophylline.

This is possible with AMINODROX because gastric disturbance is avoided.

Now congestive heart failure, bronchial and cardiac asthma, status asthmaticus and paroxysmal dyspnes can be treated successfully with oral aminophylline in the form of AMINODROX.

Aminodrox Tablets contain 1 1/2 gr. aminophylline with 2 gr. activated aluminum hydroxide.

Aminodrox-Forte Tablets contain 3 gr. aminophylline with 4 gr. activated aluminum hydroxide.

Also available with 1/4 gr. phenobarbital.



Each Cardalin tablet contains:
Aminophylline 5.0 gr.
Aluminum Hydroxide . 2.5 gr.
Ethyl Aminobenzoate 0.5 gr.
Supplied: Bottles of 100, 500, 1000. Also available, Cardalin-Phen containing ¼ gr.
phenobarbital per tablet.

Blood Levels

The therapeutic aminophylline blood levels required in bronchial asthma are now obtained with safety and simplicity with Cardalin tablets providing 5 grains of protected-aminophylline per tablet—the highest concentration supplied for oral administration. Two protective factors minimize gastric irritation.

Cardalin tablets permit institution and maintenance of effective oral aminophylline therapy also in cardiac conditions and in edematous states.

Cardalin tablets

IRWIN, NEISLER & COMPANY · DECATUR, ILLINOIS

Research to Serve Your Practice

for low-sodium



de gustibus...

By direct appeal to the palate, DIASAL enlists the willing cooperation of patients on low-sodium diets. Its exceptionally high taste equivalence to table salt is matched by close resemblance in other properties! — DIASAL looks, pours and otherwise behaves like sodium chloride at the table and in the kitchen.

Containing chiefly potassium chloride (plus glutamic acid and inert excipients). DIASAL is free from sodium, lithium and ammonium. It is accordingly sale to prescribe for prolonged and liberal use. DIASAL also serves as a prophylactic against the potassium depletion which may accompany low-sodium dieting.

DIASAL FOUGERA

seasons food like salt safely

packaging: available in 2-oz. shakers and 8-oz. bottles

Samples and low-sodium-diet sheets for your patients available on request to Professional Service Department.



E. FOUGERA & COMPANY, INC. 75 VARICE STREET, NEW YORK 13. N. Y.

- Rimmermon, A. B., and others: A Comparative Study of Sodium-free Salt Substitutes, Am. Pract. 6 Digest Treat. 2:168, 1951.
- 2. Fremont, R. E., and others: Postgrad. Med. 30:216, 1851.

clinically
accepted
for treatment
of
HYPERTENSION

VERALBA

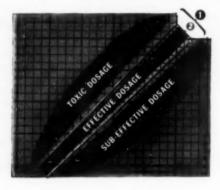
(Brand of Protoveratrines A and B)



Recent clinical investigations show that protoveratrine produces a significant decrease in systolic and diastolic blood pressures. With adequate dosage, this well-tolerated veratrum derivative can often maintain blood pressure near normal levels indefinitely, and alleviate such symptoms as headache, insomnia, delirium, dizziness, and blurred vision.

Effective dosage for the individual patient can usually be readily established with Veralba, which is available in both 0.2 mg. and 0.5 mg. grooved tablets.

Write for literature and "dose-establishment" package

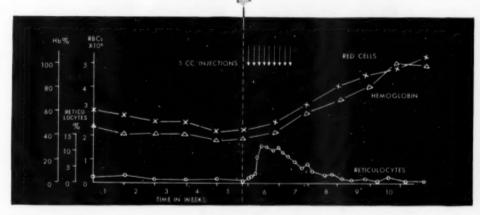


CHEMICALLY STANDARDIZED . . FOR OPTIMAL CONTROL OF DOSAGE

- The therapeutic range of protoveratrine is narrow. Hence, continued response to established dosage requires an accurately-standardized dosage form.
- ② Veralba is the only protoveratrine preparation standardized by *chemical assay*. The potency of Veralba Tablets is not permitted to vary from lot to lot by more than 3%, plus or minus.







With 'Feojectin' you can obtain a more <u>rapid</u>, a more <u>predictable</u> response than with any other iron therapy.



Indications: Clearly defined iron-deficiency anemias particularly when a prompt response is mandatory or oral administration is not feasible.

'Feojectin' is especially useful for (1) irondeficiency anemia in late pregnancy, (2) resistant iron-deficiency anemia, (3) iron-deficiency anemia in gastrointestinal disease or after G.I. tract surgery, (4) anemia in chronic bleeding hemorrhoids, menorrhagia, (5) iron-deficiency anemia before elective surgery, and (6) in selected cases, as an alternative to blood transfusion.¹

Formula: Each 5 cc. 'Feojectin' ampul contains the equivalent of 100 mg. of elemental iron, or 20 mg./cc.

Packaged: In boxes of six 5 cc. ampuls. Detailed instructions for administration accompany each box.

1. Dickstein, B., et al.: Am. J. Dis. Child. 84:52 (July) 1952.

a saccharated iron oxide for safe intravenous injection

Smith, Kline & French Laboratories, Philadelphia

#T.M. Reg. U.S. Pat. Off.



For Prevention of Angina Pectoris

Tolerance and toxicity, twin dangers of the older nitrates and nitrites, are not associated with METAMINE, the unique, new cardiac trinitrate with a nitrogen instead of the usual carbon linkage. Four METAMINE tablets daily, after meals and at bedtime, usually eliminate anginal attacks altogether or greatly reduce their number and severity. Supplied in vials of 50 tablets.

Metamine

TRIETHANOLAMINE TRINITRATE BIPHOSPHATE TABLETS, 2 MG.

Write for literature and a clinical trial supply.

Thos. Leeming & Co. Inc. 155 EAST 44TH STREET, NEW YORK 17, N. Y.

"...the
bile ducts
are
visualized
in their
natural
and
'undisturbed'



Telepaque®

Superior Oral Cholecystographic
AND CHOLANGIOGRAPHIC Medium

The frequency of bile duct visualization with Telepaque plus the high incidence of dense gallbladder shadow² are advantages of distinct diagnostic importance. Furthermore, Telepaque is notable for its low degree and percentage of side reactions.

BOSAGE: The average adult dose of Telepaque is 6 tablets with at least one glass of water from ten to twelve hours before the scheduled roentgen examination.

SUPPLIED in tablets of 0.5 Gm., envelopes of 6 tablets, boxes of 5 and 25 envelopes; bottles of 500 tablets.

WINTHROP-STEARNS INC. . Now York IS, N.Y. . Windsor, Ont.

SUSTAGEN

A NEW APPROACH TO TUBE FEEDING



PROTEIN

FAT

A COMPLETE NUTRIMENT EASILY ADMINISTERED BY TUBE

CHO

VITAMINS AND MINERALS Now for the first time optimum nutrition can be provided easily and acceptably for patients who cannot or should not take food by mouth. Sustagen and Mead's new Tube Feeding Set eliminate the traditional difficulties and hazards of tube feeding.

WITHOUT COMPLICATING SIDE EFFECTS

The diarrhea, cramps and nausea frequently caused by tube feeding mixtures have been practically nanexistent with Sustagen.

Calories Protein 910 Gm Fat Carbohydrate Vitamins and Minerals 9000 units Vitamin D. 500 unds Thismine hydrochtoride 10 mg. 100 mg Marinamuta Calcium partothingle ... 40 mg. Pyridosine hydrachlande Choline bitartrate 500 mg Vitamin B_{it} (crystalline) 4 mile Calcium 6.3 Gm. Sodium 1.0 Gm. Polassium 2 Gm.

a 94 hour feeding of 900 Gm. supplies:

Spriagen contains pre-dered whole milk, non-fall milk solids, calcium casonale and Deztri Mathuse plus vitamins and iron.

WITHOUT DISCOMPOSIT TO THE PATIENT

Mead's Tube Feeding Set provides unprecedented ease and convenience of administration. The extremely small, smooth plastic tubing, about half the size of the smallest rubber tube, is easily inserted and swallowed almost without sensation.

IDEAL ALSO FOR ORAL USE

Sustagen provides a pleasant-tasting, nutritious, well tolerated drink. A glassful made with 3 ounces Sustagen and 5 ounces water supplies 330 calories and 20 Gm. protein.

SUSTAGEN

For detailed information, write for the booklet "How to Use Sustages."

MEAD

MEAD JOHNSON & COMPANY

EVANSVILLE 21, INDIANA, U.S.A.



THE ORIGINAL ENTERIC-COATED TABLET OF THEOBROMINE SODIUM ACETATE

provides **EFFECTIVE** WELL-TOLERATED **PROLONGED** VASO-DILATION



REPEATEDLY SHOWN and proven by objective tests on human subjects1 - this is one of the most effective of all the commonly known Xanthine derivatives. Because of the enteric coating it may be used with marked freedom from the gastric distress characteristic of ordinary Xanthine therapy. Thus THESODATE, with its reasonable prescription price also, enjoys a greater patient acceptability.

> Available: In bottles of 100, 500, 1000. TABLETS THESODATE

*(7½ gr.) 0.5 Gm. *(3% gr.) 0.25 Gm.

THESODATE WITH PHENOBARBITAL

*(7½ gr.) 0.5 Gm. with (½ gr.) 30 mg. (7½ gr.) 0.5 Gm. with (¼ gr.) 15 mg.

*(3% gr.) 0.25 Gm. with (1/4 gr.) 15 mg.

THESODATE WITH POTASSIUM IODIDE

(5 gr.) 0.3 Gm. with (2 gr.) 0.12 Gm. THESODATE, POTASSIUM IODIDE WITH PHENOBARBITAL

(5 gr.) 0.3 Gm., (2 gr.) 0.12 Gm. with (¼ gr.) 15 mg.

*In capsule form also, battles of 25 and 100.

- 1. Riseman, J. E. F. and Brown, M. G. Arch. Int. Med. 60: 100, 1937 2. Brown, M. G. and Riseman, J. E. F. JAMA 109: 256, 1937.
- 3. Riseman, J. E. F. N. E. J. Med. 229: 670, 1943.

For samples just send your Rx blank marked - 7 FH10

EST. 1852

CORONARY

ARTERY

DISEASE

BREWER & COMPANY, INC.

WORCESTER B. MASSACHUSETTS U.S.A.

rondition	meidener of liver dysfunction	incidence of blood lipid abnormalities	suggested therapy
obesity	frequent	frequent	Methischol plus balanced low calorie diet.
diabetes		frequent	Methischol as adjunct to diet. Insulin as necessary.
atherosclerosis			Methischol and high protein, low fat diet.
coronary disease			Methischol as adjunct to high protein, low fat diet and specific therapy.
alcoholism			Methischol plus high protein diet.

methischol

the <u>complete</u> lipotropic therapy

... because it provides vitamin B₁₂ and liver fractions in addition to choline, methionine and inositol.

... helps normalize liver function, increase phospholipid turnover, reduce fatty deposits, and stimulate regeneration of new liver cells...

...helps reduce elevated cholesterol levels and chylomicron ratios towards the normal, and aids in achieving normal fat metabolism.

in d

therapeutic dose of 9 capsules or 3 tablespoonfuls of Methischol provides:

the suggested daily

Choline Dihydrogen
Citrate* 2.5 Gm.

dl, Methionine 1.0 Gm.
Inositol 0.75 Gm.

Vitamin B₁₂ 18 mcg.

Liver Concentrate and Desiccated Liver** 0.78 Gm.

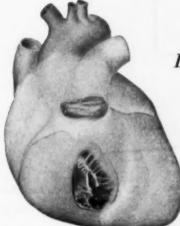
*Present in syrup as 1.15

U. S. Vitamin corporation

for samples and

casimir funk labs., inc. (affiliate) 250 E. 43 St. • New York 17, N.Y. Gm. Choline Chloride
**Present in syrup as 1.2
Gm. Liver Concentrate

HydroCortisone, MERCK) BYDROCORTISONE, MERCK)



Lifesaving agent
in acute
Rheumatic Fever
with Carditis

Every patient suffering from rheumatic fever with carditis should receive the benefits of HYDROCORTONE. Its suppressive action on severe carditis has been lifesaving.

Reports state that early and adequate therapy in carditis appears to prevent valvulitis; congestive failure due to acute carditis often is controlled when salt intake is limited; and extracardiac manifestations show striking clinical improvement.

Active research is under way to determine whether this treatment prevents development of chronic valvular disease.

Literature on request

HYDROCORTONE is the registered trade-mark of Merch & Co., Inc. for its brand of hydrocortisone.



MERCK & CO., INC.

Manufacturing Chomists

proven

pain

control

with safety

to the need

ed degree desired

'EMPIRIN'

COMPOUND

with Codeine Phosphate

Sulgen to Pederal Narcotle Lab

No. 1 - 25 gr.

No. 3 - 16 ov.

No O ... Id me

The Aunt on

BURNOUSHS WELLOWING & CO. ID. S. A. ONL. Tribules 7, Nov York



an improved approach to ideal hypotensive therapy

Low toxicity. The only hypotensive drug that causes no dangerous reactions, and almost no unpleasant ones.

Slow, smooth action. The hypotensive effect is more stable than with other agents. Critical adjustment of dosage is unnecessary. Tolerance to the hypotensive effect has not been reported.

Well suited to patients with relatively mild, labile hypertension. A valuable adjunct to other agents in advanced hypertension.

Bradycardia and mild sedation increase its value in most cases. Symptomatic improvement is usually marked.

Convenient, safe to prescribe

The usual starting dose is 2 tablets twice daily. If blood pressure does not begin to fall in 7 to 14 days, and the medication is well tolerated, the dose may be safely increased. Should there be a complaint of excessive sleepiness, the dose should be reduced. Some patients are adequately maintained on as little as one tablet per day.

Dosage of other agents (veratrum or hydralazine) used in conjunction with Raudixin must be carefully adjusted to the response of the patient. If Raudixin is added to another maintenance regimen, the usual dose is applicable, and it is often possible to reduce the dose of the other agent or agents.

Supplied in tablets of 50 mg., bottles of 100 and 1000.

SQUIBB

RAUDIXIN
RQUIBB RAUWOLFIA BERFENTINA
Tablets

"RAUDININ" IS A TRADEMARS



Mealtime Variety for SODIUM RESTRICTED DIETS

LOW SODIUM CHEESE—Tasty cheese with sodium content less than milk—only 9.5 mg. per 100 grams. Makes delicious rarebit with Cellu Tomato Puree.

CELLU TOMATO PUREE—Packed in strained form, without added salt or other seasoning. Only 8 mg. sodium in 100 grams. For many flavorsome dishes.

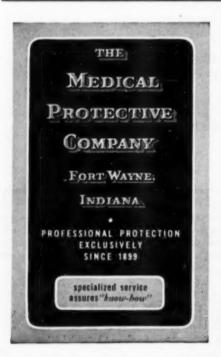
Send for Free Catalog

CELLU SODIUM RESTRICTED

Dietary Goods

CHICAGO DIETETIC SUPPLY HOUSE Inc.

1750 West Van Ausen Mirest Chicago 13, Illinese



CAN YOU ANSWER These Vital CARDIO-RESPIRATORY FUNCTION QUESTIONS?

- ★ Why are standard vital capacity procedures insufficient in chronic pulmonary disease?
- ★ How important are "timed" vital capacity measurements?
- ★ What is the length of time recommended for the MBC test?
- ★ How is a patient's normal MBC figured?
- ★ What are the three important function measurements relating to the mechanical aspects of pulmonary aeration?
- What two simple screening tests (taking only five minutes) give ample information to detect early lung function abnormalities even before subjective or roentgenologic changes are apparent?
- ★ What percentage below normal can MBC and VC be before further studies are necessary?

THIS JUNE, 1953 REPRINT

HURLEY L. MOTLEY, Ph.D., M.D.

Professor of Medicine and Director of the Cardio-Respiratory Laboratory, University of Southern California, entitled, "Detection of Early Lung Function Changes in Industrial Exposure," has the answers to the above questions and many more. It explains the simple tests that can disclose early lung function disorders that are suitable for annual or preemployment screening.

MAIL COUPON FOR YOUR FREE COPY TODAY

Gent Pleas abou							1	75	e	,	t	h			8	ı	b	0	v	e		1	ej	p	ri	n	3			n	d		í	ı	ıf	0	n	n	a	ti	io	6
		R	18	p	ù	10	m	n	8	ŧ			t	I	1	h		1.4			1	г	١	1	r	e	n	æ	đ	3	71	Ł	a	le	94	n oi		te	ır			
Dr.		. ,										,									,	,							×													
St												0																												0	4	
City																			8-			. ,												1	21	91	14	١.	,		,	
State	,					0	٠					0			0	0						0						0	0						0				0			0 4

Estrogen and androgen go together
like "compass and pen"
to provide a dual approach
for maximum efficiency
in dysmenorrhea.
Many clinicians feel
that these two steroids,
together, as combined in
"Premarin" with Methyltestosterone,
are more effective

than either one alone

Excellent results have been reported

in producing relief of pain by suppressing ovulation.

from such therapy.

"PREMARIN" with METHYLTESTOSTERONE

for combined estrogen-androgen therapy



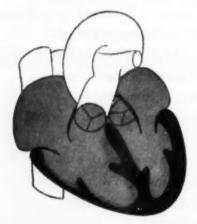
Ayerst, McKenna & Harrison Limited · New York, N. Y. · Montreal, Canada

NOW

the first intramuscular digitoxin

DIGITALINE NATIVELLE' INTRAMUSCULAR

for dependable digitalization and maintenance when the oral route is unavailable



DIGITALINE NATIVELLE INTRAMUSCULAR

is indicated for patients who are comatose, nauseated or uncooperative, or whose condition precludes the use of the oral route.

DIGITALINE NATIVELLE

INTRAMUSCULAR
provides all the unexcelled virtues of
its parent oral preparation.
Steady, predictable absorption.
Equal effectiveness, dose-for-dose
with oral DIGITALINE NATIVELLE.
Easy switch-over to oral medication.

Clinical investigation has shown that DIGITALINE NATIVELLE INTRAMUSCULAR is "effective in initiation and maintenance of digitalization. A satisfactory therapeutic effect was obtained with minimal local and no undesirable systemic effects."*

DIGITALINE NATIVELLE INTRAMUSCULAR - I-cc. and 3-cc. ampules, boxes of 6 and 50. Each oc. provides 0.3 mg. of the original digitoxin - DIGITALINE NATIVELLE.

*Strauss, V.; Simon, D. L.; Iglauer, A., and McGuire, J.: Clinical Studies of Intramuscular Injection of Digitaria (Digitaline Nativelle) in a New Solvent, Am. Heart J. 44:787, 1952.

Literature and samples available on request.

VARICK PHARMACAL COMPANY, INC. (Division of E. Pougera & Co., Inc.) 73 Varick Street, New York 13, N. Y. Upjohn

cortisone for inflammation, neomycin for infection:

Each gram contains:

Cortisone Acetate 15 mg.

Neomycin Sulfate 5 mg.

(equivalent to 3.5 mg. neomycin base)

Available in 1 drachm tubes with applicator tip

The Upjohn Company, Kalamazoo, Michigan



Neosone



EVENTUALLY, you may be riding herd on his irregular

vides six important B vitamins, plus liver fraction and brewer's yeast. Sur-bex with C adds five times the minimum daily requirement of ascorbic acid.

> No trace of liver odor in these triple-coated, vanillaflavored tablets. Daily prophylactic dose is one tablet. Two or more for severe deficiencies. In bottles abbott

SUR-BEX Tablet contains:

			monitra					
	Ribofis	win					6 r	ng
	Nicotii	namide				8	10 t	ng
	Pyrido	zine H	ydroch	loride.			1 1	Di
-	Vitami	n B12 (as vita	min B	8			
	eone	entrate	1)			1	m	eg
	Pantot	benie /	Acid (a	s calciu	m			-
	pant	othena	(e)			1	0 n	N
	Liver I	ractio	n 2, N.	F., 0.3	1 Gr	m. (1	gr	8.
	Brower	'я Уем	et, Drie	rd .			-	
				0.18 (lm.	(21/2	gr	8.
	tur.ber	milit. 9	(damin	C anni	nine	150	1 .	

PRESCRIBE

of 100, 500 and 1000.

or SUR-BEX with C

A COMPARISON OF SULFONAMIDE PREPARATIONS:

Capacity to Produce Adequate, Sustained Blood Levels

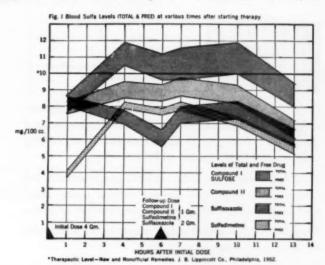
From a Recent Report: "The Effect of an Alumina Gel Vehicle on the Blood Level of a Triple Sulfonamide Preparation after Oral Administration."

"In accordance with the standards established by the Council on Pharmacy and Chemistry of the American Medical Association² regarding therapeutic blood levels, it was deemed advisable to judge the effectiveness of the various preparations on the basis of their ability to provide sustained blood sulfonamide concentrations of 10 to 15 mg. per 100 cc."

Four sulfonamide preparations were studied:

- (a) SULFOSE*—triple sulfonamides in alumina gel suspension
- (b) Compound II—triple sulfonamides without alumina gel
- (c) Sulfisoxazole tablets
- (d) Sulfadimetine tablets

For details on dosage and comparative blood levels obtained, see chart below.



RESULTS

- Only one preparation—SULFOSE produced average blood levels exceeding 10 mg. total sulfonamides per 100 cc.
- 2. Average acetylation was moderate for all preparations, ranging around 10 per cent (±5 per cent).
- Triple sulfonamides produce greater and better sustained blood levels.
- 4. Sulfose—triple sulfonamides in alumina gel suspension—provided both

"higher initial as well as more prolonged therapeutic levels . . . "

SULFOSE®

Triple Sulfonamides

SUPPLIED: Suspension, bottles of 1 pint. Each 5 cc. teaspoonful contains 0.167 Gm. each of sulfadiazine, sulfamerazine and sulfamethazine in a special alumina gel vehicle.

Also available: Tablets, bottles of 100 and 1000.

References: 1. Berkowitz, D.: Antibiotics & Chemotherapy 3:618 (June) 1953.

2. New and Nonofficial Remedies.

J.B. Lippincott Company, Philadelphia,



Philadelphia Z, Pa.

1952, p. 103.

the realization of a hope ...

a new physio-chemical complex

normalizing cholesterol metabolism

MONICHOL*





One out of every 6.3 cardiovascular patients

One out of every 4.1 diabetic patients has hypercholesteremia.t

Recent studies have proved that Monichol*, generally normalizes elevated blood cholesterol levels. Patients treated showed a *significant* drop of serum cholesterol levels ranging from 59 to 233 mg. per 100 ml.†

Monichol, therefore, is indicated both prophylactically and therapeutically in patients showing elevated serum cholesterol levels associated with cardiovascular disease and diabetes.

Monichol has cholesterol lowering properties not attributable to any of its component parts.

Monichol, in the experience of the investigators, has proven to be entirely non-toxic.

Monichol normalizes cholesterol metabolism

Formula: Each teaspoonful (5 cc.) of Monichol contains:

Polysorbate 80 500 mg. Choline Dihydrogen Citrate 500 mg.

Inositol 250 mg.

Dosage: 1 tsp. (5 cc.) 4 times daily or 2 tsps. twice daily after meals.

Supplied: In bottles of 12 oz.

Literature available on request.

IVES-CAMERON COMPANY, INC., 22 East 40th Street, New York 16, N. Y.

†Sherbst, D. A., and Levites, M. M.: Hypercholesteramia. Effect on Cholesterol Metabolism of a Polysorbate 80-Choline-Inositol Complex (MONICHOL) J.A.M.A. 152:682 (June 20) 1953. *Trademark

Over a Quarter Century of Service to the Medical Profession

for greater carbohydrate alimentation ... prescribe

10% Travert squitions

- · for twice the calories of 5% Dextrose
- · in equal infusion time
- · with no increase in fluid volume

With 10% Travert solutions, a patient's carbohydrate needs can be more nearly satisfied within a reasonable time and without excessive fluid volume or vein damage. • Travert solutions are sterile, crystal-clear, colorless, non-pyrogenic and non-antigenic. They are prepared by the hydrolysis of cane sugar and are composed of equal parts of D-glucose (dextrose) and D-fructose (levulose). Travert solutions are available in water or saline in 150 cc., 500 cc., 1000 cc. sizes.

Re

"Travert" trademark of BAXTER LABORATORIES,

products of

BAXTER LABORATORIES, INC.

Morton Grove, Illinois . Cleveland, Mississippi

DISTRIBUTED AND AVAILABLE ONLY IN THE 37 STATES EAST OF THE ROCKIES (except in the city of El Paso, Texas) THROUGH

AMERICAN HOSPITAL SUPPLY CORPORATION

GENERAL OFFICES . EVANSTON, ILLINOIS



PHOTOGRAPH BY PAUL RADKAL

Easy-to-administer oral antibacterial therapy

PENTRESAMIDE-250

TRIPLE SULFONAMIDE WITH PENICILLIN

ACTIONS AND USES: PENTRESAMIDE Tablets provide the combined antibacterial activity of penicillin and sulfonamides—in many susceptible infections more effective than either agent used alone. They are especially useful in mixed infections.

SUPPLIED: Tablets in bottles of 60 and 250. Granules for suspension in water in dispensing bottle containing 6 Gm. triple sulfonamide and 3,000,000 units buffered penicillin G. One tablet or one teaspoonful of suspension provides: 0.1 Gm. sulfamerazine, 0.2 Gm. sulfadiazine, 0.2 Gm. sulfamethazine and 250,000 units of potassium penicillin G.

DOSAGE: Adults, 1 or 2 tablets or teaspoonfuls q.i.d. Children, by weight and condition. Dosage schedule on request.

Carynebacterium diphtheriae Bacillus anthracis Clostridia Staphylococcus Streptococcus Meningacoccus Meningacoccus Brutelia abortus Escherichia coli Aerobacter aerogenes Proteus vulgaris Shigelia Pseudomonas Berthelia typhosa Salmonelia

ANNALS OF INTERNAL MEDICINE

VOLUME 39

OCTOBER, 1953

NUMBER 4

ASEPTIC MENINGITIS, A DISEASE OF DIVERSE ETIOLOGY: CLINICAL AND ETIOLOGIC STUDIES ON 854 CASES *

By Charles V. Adair, Captain, MC, USA, Ross L. Gauld, M.D., and Joseph E. Smadel, M.D., Washington, D. C.

Sporadic cases of infection of the central nervous system, presumably of viral origin, contribute much of the material received by a virus diagnostic laboratory. The present report is concerned with an analysis of material of this type submitted over a period of 11 years from military personnel, veterans and their dependents in the United States. Almost all of the 854 patients who provide the basis of this study presented clinical findings resembling the syndrome designated by Wallgren as acute aseptic meningitis. In only a few of the patients was the clinical picture indicative of deep-seated neurologic involvement compatible with the diagnosis of encephalitis.

The criteria which Wallgren established for the syndrome aseptic meningitis are listed in table 1. He was cognizant in 1925 of the similarity of the clinical features of this entity to the meningeal symptoms of tuberculous meningitis, poliomyelitis, epidemic encephalitis, mumps, typhoid fever, Weil's disease, syphilis and helminthiasis. Subsequent experience has shown that, in addition to the infections considered by Wallgren, a number of others may at times simulate his syndrome. Most of the neurotropic viruses are assumed to be potentially capable of producing aseptic meningitis; however, among those that have been incriminated more frequently are the agents of lymphocytic choriomeningitis, encephalomyocarditis, the Coxsackie group, herpes simplex, type 2 poliomyelitis and certain of the viruses responsible for the arthropod-borne encephalitides.

The present report is concerned primarily with the clinical and clinical laboratory findings in groups of cases of aseptic meningitis caused by the

*Received for publication April 15, 1953.

From the Department of Virus and Rickettsial Diseases, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D. C.

agents of lymphocytic choriomeningitis, mumps, herpes simplex and leptospirosis, and with the incidence of these specific infections in a large series of sporadic cases of acute aseptic meningitis.

TABLE I

Wallgren's Criteria for Aseptic Meningitis*

- I. Acute onset with obvious signs and symptoms of meningeal involvement.
- Alteration of cerebrospinal fluid typical of meningitis. The cerebrospinal fluid may show a small or large number of cells.
- Absence of bacteria in cerebrospinal fluid, as demonstrated by appropriate direct or cultural technics.
- IV. Relatively short benign course of illness.
- V. Absence of local parameningeal infection (otitis, sinusitis, trauma, etc.), or a general disease which might present meningitis as a secondary manifestation.
- VI. Absence from the community of epidemic disease of which meningitis is a feature.
 - * Paraphrased from a direct translation from the French.1

In a rapidly developing field such as that covered by a virus diagnostic laboratory, the procedures used to establish the etiology of cases of aseptic meningitis have undergone changes during the 11 year period of the current study. These laboratory problems, which are discussed elsewhere, are not the principal concern of the present report. However, sufficient information is provided to indicate the technics and the criteria employed for interpreting the results obtained.

MATERIALS, METHODS AND INTERPRETATION OF TESTS

Clinical Materials: The most common clinical diagnoses made on the patients at the time specimens were submitted to the virus laboratory were as follows: virus meningitis, encephalitis, meningo-encephalitis, aseptic meningitis, lymphocytic choriomeningitis, nonparalytic poliomyelitis, and virus infection of the central nervous system.

The 854 cases included in the present analysis were culled from approximately 1,300 cases on whom materials were received for laboratory diagnostic studies. Excluded from the analysis were those on whom inadequate records and insufficient or unsuitable specimens were available. The 854 patients chosen had the following in common: (1) the clinical features of the illness resembled those described by Wallgren as listed in table 1; (2) serum specimens submitted for diagnostic study were collected at an optimal time in the course of the patient's illness so that antibodies resultant from the acute disease under consideration might be expected to be present. In about three-quarters of the instances, paired specimens of serum were obtained, one taken in the first week of the illness and the second taken three to four weeks after onset of the illness. In addition, a third specimen of serum collected six to eight weeks after onset of the illness was often available.

All sera were frozen on receipt in the laboratory and maintained at -20° C. except when thawed for testing. Attempts to isolate the etiologic agent from the cerebrospinal fluid, brain or blood were made in those instances in which suitable materials were properly submitted to the laboratory for isolation purposes.

The hospital charts of the cases which proved to be positive by laboratory procedures for lymphocytic choriomeningitis, mumps, herpes simplex and leptospirosis were obtained and carefully reviewed. The essential features of the history, physical examination, laboratory findings, hospital course, complications and residual effects of the acute illness were tabulated.

Laboratory Procedures: Lymphocytic Choriomeningitis: Sera from 828 cases were studied for two types of antibodies against the virus of lymphocytic choriomeningitis (LCM) by means of the complement-fixation 8 and neutralization tests.4 Fixation of complement at an initial serum dilution of 1:2 in the presence of two units of the soluble antigen obtained from the spleens of LCM infected guinea pigs was regarded as a positive serologic result, but a fourfold rise in antibody titer in paired specimens of sera was considered a more reliable criterion of infection. The presence of antibodies which neutralized 100 or more LD50 of a known standard challenge strain (WE) in the mouse neutralization test was considered diagnostic of infection, remote or recent, with the virus of LCM. However, a diagnosis was considered to be established definitely by the neutralization technic only if the convalescent serum, in addition to neutralizing 100 or more LD50 of the standard strain of LCM virus, protected against an additional 10 or more LD_{50} of the standard virus than the acute phase serum. In all instances but one in this series, paired sera from single patients were tested in the same protocol, thereby limiting the range of laboratory error. In certain cases, neutralizing antibodies were present at diagnostic levels in both acute and convalescent serum specimens, with no demonstrable increase in antibody in the second specimen. In these instances, unless the diagnosis was established by other means the antibodies were presumed to have resulted from a previous infection with the virus of LCM and to be unrelated to the present clinical illness. Certain of these sera were tested for the presence of Merthiolate (which might have been added by outlying installations as a preservative agent),* following the demonstration by Rogers 5 that Merthiolate in human serum inactivates LCM virus and gives falsely positive neutralization tests. In the absence of other confirmatory tests, cases were excluded from the study if their sera gave a positive neutralization test for LCM but contained detectable amounts of Merthiolate. Those cases in which the single convalescent serum available contained diagnostic levels of neutralizing antibodies and no Merthiolate, and in which the clinical history was satisfactory, were considered as possibly due to LCM.

^{*}Tests for Merthiolate in specimens of serum were kindly done by Dr. Leo R. Goldbaum, of the Department of Biochemistry of the AMSGS.

In certain cases an attempt was made to isolate LCM virus from blood and spinal fluid obtained from patients during the early stages of illness or, if dead, from brain tissue obtained at autopsy. Guinea pigs and adult white mice were injected intracerebrally and intraperitoneally with such materials and carefully followed for signs of illness. Rectal temperatures were taken daily on each of the guinea pigs; the mice were carefully observed for signs of central nervous system disease. If illness occurred in any of the animals, further passages were made as indicated; the agent was identi-

fied by the technic of Smadel and Wall.6

Mumps: Sera from 819 cases were examined by the complement-fixation technic for serologic evidence of infection due to the mumps virus. Antigen was prepared from parotid gland tissue of monkeys infected with the Enders strain of mumps virus. Serum antibody titers were expressed as the highest initial dilution of serum which gave complete or almost complete fixation of complement in the presence of two units of the mumps antigen. A fourfold rise in antibody titer in paired serum specimens was considered diagnostic of recent infection with the mumps virus. In those instances in which only convalescent serum was available for study, a titer of 1:64 was considered diagnostic, a titer of 1:32 presumptive; but a titer of 1:16 or less was not regarded as indicative of recent infection. It should be noted that our complement-fixing titers are calculated on the basis of actual dilution of serum, in contrast to the procedure of Enders and Cohen, which employed final dilution; hence, a value of 1:32 in our hands corresponds to one of 1:96 in Enders' laboratory.

Isolation of the mumps virus was attempted in only a few instances. For this procedure spinal fluid was inoculated into the amniotic sacs of seven day old embryonated hen's eggs. Mumps virus was recovered from one patient; the agent was identified by the agglutination of human "O" red blood cells by infected amniotic fluid and inhibition of this hemagglutination

by mumps convalescent human serum."

Herpes Simplex: The egg neutralization test ¹⁰ was used to demonstrate antibodies against the virus of herpes simplex. Those cases in which neutralizing antibodies were absent in the acute phase serum and present in the convalescent phase serum were considered to be caused by infection with the virus of herpes simplex. In each case of primary herpes simplex meningitis with such a pattern of antibody response, the results were reproducible in three separate neutralization tests. The "all or nothing" principle of neutralizing antibody response to herpes simplex infection propounded by Burnet ¹¹ was recognized and no attempt was made to titrate the amount of antibody present in the sera. In no instance in this series was the virus of herpes simplex isolated from the body fluids or tissues submitted for such purpose.

Five of the six cases diagnosed as primary herpes simplex infection on the basis of serologic findings were found in a group of 77 patients chosen at random by sampling cases of undiagnosed central nervous system disease that had been previously studied serologically and found negative for LCM and mumps infections. The remaining case was detected among 37 cases of aseptic meningitis studied from June, 1951, to June, 1952. In this last period, neutralization tests for herpes simplex infections were included as an

integral part of the diagnostic study of cases of aseptic meningitis.

Leptospirosis: Serologic tests for a wide spectrum of serotypes of leptospires, using the microscopic agglutination-lysis test, 12, 13 were performed by the Veterinary Division of the Army Medical Service Graduate School. Diagnosis of infection with one of these serotypes was regarded as established if a fourfold increase in antibody titer was demonstrable during convalescence. A presumptive diagnosis was made if antibodies were present in a titer of 1:400 or greater in the early convalescent stage of central nervous system illness. Nine cases of leptospiral meningitis were found in a random sample of 91 patients with aseptic meningitis who failed to yield serologic evidence of infection with LCM or mumps viruses. The remaining three cases were detected among 67 cases of aseptic meningitis studied between June, 1951, and June, 1952. During this time serologic tests for leptospiral infections were included as part of the diagnostic studies on all cases of aseptic meningitis.

Other Agents: There were 634 patients in whom no evidence was found for infection with one of the agents listed above. Sera from these cases were tested, in certain instances, for antibodies against other infectious agents. Examinations for viral neutralizing antibodies were made as follows: 78 patients, Western equine encephalomyelitis; 71, St. Louis encephalitis; 59, Eastern equine encephalomyelitis; 19, members of the Coxsackie group; 10, encephalomyocarditis; 5, Japanese encephalitis; 4, Colorado tick fever; 2, West Nile disease; 2, Venezuelan equine encephalomyelitis; 1, Russian spring-summer encephalitis. Complement-fixation tests were performed on sera from 22 patients for antibodies against the psittacosis-lymphogranuloma venereum group of viruses and for antibodies against the rickettsial diseases Q fever, Rocky Mountain spotted fever and rickettsial-pox in 10, 2 and 1 instances, respectively. In addition, tests for antibodies against toxoplasma were made on sera from two patients and for heterophil agglutinins in 13 instances. All these tests were negative.

RESULTS

Incidence of Diagnosed Infections: The 854 cases studied in the 11 year period, 1941–1952, fall into three general groups on the basis of time of occurrence and extent of laboratory studies. Sera collected during the period 1941 to 1946 were employed in tests for LCM and mumps, but the stored frozen specimens were not examined in later years for antibodies against herpes simplex or leptospires. The incidence of LCM and mumps

TABLE II

Incidence of Lymphocytic Choriomeningitis and Mumps Among 374 Cases of Aseptic Meningitis Studied at the Army Medical Service Graduate School, 1941-1946*

	Number	Per Cent
Proved Cases:		
Lymphocytic Choriomeningitis	32	8.5
Mumps	22	5.9
Possible Cases:		
Lymphocytic Choriomeningitis	10	2.7
Mumps	35	9.4
Aseptic Meningitis of Unknown Etiology	275	73.5
Total Cases	374	100.0

* Data reproduced from Rasmussen.14

in the 374 cases of aseptic meningitis studied from 1941 to 1946 by Rasmussen 14 is indicated in table 2.

Practically all of the 480 cases studied between 1947 and 1952 were subjected to diagnostic tests for LCM and mumps. Laboratory procedures for herpes simplex and leptospirosis were introduced into the diagnostic armamentarium in 1951 and subsequently employed in all cases of aseptic meningitis from whom suitable specimens were obtained. However, prior to this these procedures had been applied only to stored sera selected at random from cases studied between 1947 and 1950 and found to give negative results for LCM and mumps. The incidences of these four infections in the cases examined after 1947 are given in table 3.

Of 454 cases listed in table 3 who were tested for antibodies against LCM, 37 (or 8.1 per cent) were unequivocally positive; an additional 7 (or 1.6 per cent) were probably positive; thus, the total crude incidence rate was 9.7 per cent. The seven probable cases of LCM included those who supplied only a single convalescent serum; however, these specimens were free of Merthiolate and contained sufficiently large amounts of neutralizing substances to indicate recent experience with the agent of LCM.

TABLE III

480 Cases of Aseptic Meningitis, Percentage of Cases Diagnosed in the Laboratory, Army Medical Service Graduate School, 1947–1952

Diagnosis	Number Cases	Proved	1 Cases	Probab	le Cares	No.	Total Cases	Percentag
L/IME ISONES	Tested	No.	%	No.	%	240.	Minimal ¹	Maximal ²
LCM Mumps Herpes Leptospirosis	454 445 114 158	37 42 6 12	8.1 9.4 5.3 7.6	7 17 —	1.6 3.9	44 59 6 12	9.2 12.3 1.2 2.5	9.7 13.3 5.3 7.6
Total	480						25.2	35.9

¹ Percentage of 480 cases actually diagnosed.

⁸ Percentage of 480 cases which would have been diagnosed if the proportions in those tested had applied to the entire group.

Forty-two of the 445 cases tested for antibodies of mumps gave unequivocally positive results, i.e., a fourfold increase in antibodies during convalescence, or an antibody titer of 1:64 or greater in one of the convalescent sera. Seventeen additional cases were possibly due to mumps. In such instances a titer of 1:32 was obtained in one or more serum specimens tested. Thus, a total of 13.3 per cent of this group of cases of aseptic meningitis were considered to be caused by the virus of mumps.

One hundred and fourteen cases were tested for neutralizing antibodies against herpes simplex virus. Six (or 5.3 per cent) of these patients presented serologic evidence of a primary herpes simplex infection. In each of the six, neutralizing antibodies were absent in the first serum specimen and present in the second. Twelve of the 158 patients tested for antibodies against a variety of serotypes of leptospires were shown to have suffered from disease caused by a member of this group of microbial agents.

Since not all of the 480 patients mentioned in table 3 were subjected to laboratory tests for the four agents commonly employed in this study, one cannot make exact statements regarding the incidences of LCM, mumps, herpes simplex and leptospirosis in the total group. However, it is possible to obtain minimal and maximal percentages for the incidence of each type of infection in the group. The former could be calculated on the basis of the actual number of proved cases of each disease among the total 480 patients in the series, and the latter on the basis of the per cent of positives among the group actually tested. Values obtained by both methods of calculation are given in table 3.

Lymphocytic Choriomeningitis: Clinical Picture: The clinical findings in 79 * cases of LCM diagnosed between 1941 and 1952 are summarized in table 4. These include all 69 proved cases and 10 of those listed as pos-

sible LCM in tables 2 and 3.

The predominant symptoms and signs in this group of cases were headache, fever and stiff neck. It is worthy of note that not all cases of LCM developed nuchal rigidity as part of the clinical disease. However, in these instances other features of the illness were sufficiently suggestive of central nervous system disease to warrant a diagnostic lumbar puncture. The febrile period during the meningeal phase of illness lasted an average of 5.8 days. Nausea and vomiting were frequent symptoms and, to a lesser extent, malaise, myalgia and minor aches and pains. Only 20.8 per cent of the cases presented abnormalities other than nuchal rigidity upon neurologic examination. In five instances the deep tendon reflexes were hyperactive, and in seven they were hypoactive or absent; in only four instances was there muscle weakness or paralysis. Two of the patients with muscle paralysis subsequently died. Irritability, restlessness, tremor, confusion, nystagmus and vertigo were uncommon. Twenty and two-tenths per cent of the cases presented signs of involvement of the respiratory tract, such

^{*} One of these cases has been reported elsewhere by Havens.18

as sore throat and cough. In two instances râles were heard on auscultation of the chest, but in no instance was there pulmonary consolidation as demonstrated by x-ray; this is of interest, as will be discussed later. Conjunctivitis, photophobia, abdominal pain and backache were present in a relatively small number of cases.

In view of the observation by Lépine, Mollaret and Kreis ¹⁶ that the clinical disease, LCM, occurred in two or more febrile episodes and that the meningitic phase usually occurred with the second appearance of fever, it was of interest to determine how many of these 79 cases of LCM gave a history of a prodromal illness prior to their meningeal disease. To be sure,

TABLE IV

Frequency of Signs and Symptoms in Laboratory Confirmed Cases of Lymphocytic Choriomeningitis, Mumps Meningitis, Herpes Simplex Meningitis and Leptospiral Meningitis Army Medical Service Graduate School, 1941–1952

		LCM		Mum	ps Menin	gitis		erpes		ospiral
	Nu	mber	Per Cent	Nu	mber	Per Cent		ningitis mber		ingitis imber
	Total*	Positive	Cent	Total*	Positive	Cent	Total*	Positive	Total*	Positive
A. General										
1. Headache	76	75	98.7	77	7.5	97.4	6	5	12	11
2. Stiff neck	77	70	90.9	81	69	85.2	6	5	12	10
3. Fever	78	77	98.7	84	83	98.8	6	6	12	12
4. Average duration of fever	58	5.8 days		70	7.3 days		6	13 days	11	7.9 days
Nausea and/or vomiting	79	52	65.8	71	47	66.2	6	4	12	6 7
 Malaise, weakness, aches, pains 	79	28	35.4	86	18	20.9	6	3	12	7
7. Abnormal neurologic findings	77	16	20.8	84	20	23.8	6	4	12	2
8. Respiratory involvement	79	16	20.2	86	11	12.8	6	0	12	4
9. Conjunctivitis-photo- phobia	79	15	19.0	86	6	6.9	6	0	12	4 2
10. Abdominal pain	79	7	8.9	86	12	14.0	6	0	12	0
11. Backache	79	11	13.9	86	11	12.8	6	0	12	0
B. State of Consciousness	74			76			6		12	
1. Alert		52	70.2		48	63.1		3 3		11
2. Drowsy, lethargic, sompolent		18	24.3		18	23.7		3		1
3. Semi-coma		2	2.7	1	8	10.5		0		0
4. Coma		2 2	2.7		8 2	2.6		0		0

^{*} Number with sufficient data to interpret.

this prodrome often was not recognized by patients or, if recognized, was not duly recorded in his chart upon admission to the hospital. However, at least 35.5 per cent of these cases presented a definite history of a prodromal illness occurring on the average of 10 days prior to the onset of meningitis. In two-thirds of these cases the prodromal symptoms were influenza-like in nature, with generalized aches, pains and malaise. In the other one-third prodromal symptoms were those of a sore throat or a mild upper respiratory infection.

Of interest also as a measure of the severity of the illness was the degree of alteration of the normal state of consciousness of the patient during the course of acute central nervous system illness. Seventy and two-tenths per cent of this group of patients remained fully alert during the acute illness; 24.3 per cent were noted to be drowsy, lethargic or somnolent; only 2.7 per cent were semicomatose; another 2.7 per cent were comatose. The latter two patients, however, were comatose only for a brief period prior to death.

Complications and residuals of the acute disease were few. One patient suffered a pulmonary embolism on the tenth day of illness. It is doubted that this was related to the primary disease per se. One patient noted a persistent fine tremor of the hands, hyperhidrosis, headache and backache three months after the onset of the illness. Two patients were subsequently found to have Parkinsonism. One was discovered six months after his illness, and the other was noted to have typical Parkinsonism two years after apparent recovery from LCM. Diagnoses in both cases were made by Army Physical Evaluation Boards prior to their discharge from military service. Two patients died of LCM, 14 and 19 days after the onset of their respective illnesses. One presented a picture similar to Landry's ascending paralysis and died of respiratory paralysis; the other presented the findings of bulbar paralysis with respiratory failure. In both cases the diagnosis was established by isolation of the virus of LCM from the brain obtained at autopsy and confirmed in one instance by the presence of complement-fixing antibodies for LCM in serum drawn from the patient three days before his death. Following is a brief account of one case of LCM observed in this series of cases

CASE REPORT

Case 1. A 13 year old white female was admitted to an Army Hospital on December 22, 1946, with the chief complaint of fever, headache and vomiting. From December 12 to December 16 she had been mildly ill with a headache and fever; her temperature ranged around 101° F. On December 20 the headache recurred and was accompanied by slight nuchal rigidity, nausea, vomiting and a fever of 103° F. With persistence of these symptoms the patient was admitted to the hospital on December 22. Physical examination was essentially negative; no neurologic abnormalities were noted. Laboratory findings were as follows: white blood cell count, 9,500; differential count: segmented forms, 66 per cent; lymphocytes, 34 per cent; cerebrospinal fluid collected on admission to the hospital showed 1,700 cells/c.c., of which 96 per cent were lymphocytes; globulin, 4 plus; sugar, 78 mg. per 100 c.c., and chloride, 527 mg. per 100 c.c. On December 23 the headache was less severe but nausea and vomiting persisted. A chest x-ray on the following day was normal. After December 26 the patient was asymptomatic; no neurologic abnormality was noted at any time. Subsequent laboratory studies were as denoted in figure 1. Spinal fluid and blood collected on December 24, the fifth day of central nervous system illness, were pooled and injected into two guinea pigs and six adult white mice. The first guinea pig became febrile on the third day and was sacrificed on the seventh day after inoculation. Its brain was passed to normal and LCM immune guinea pigs; its spleen contained the soluble specific antigen of LCM virus. The normal passage animals all sickened and three of four died, while the immune guinea pigs ran a completely afebrile course for 26 days. The second guinea pig of the original pair inoculated with human material became febrile on the third day and died on the sixteenth day after inoculation. Its brain was passed to six adult mice,

all of which became ill seven days later. They were sacrificed and their spleens also were found to contain soluble specific antigen of LCM virus. All six mice inoculated with the original material sickened; two were passed to normal and two to LCM immune mice, with death on the seventh to tenth days of all normal mice, and no sign of disease for 28 days among the immune mice. The results of complement-fixation and neutralization tests made on serum taken from the patient at intervals during her illness are presented in figure 1.

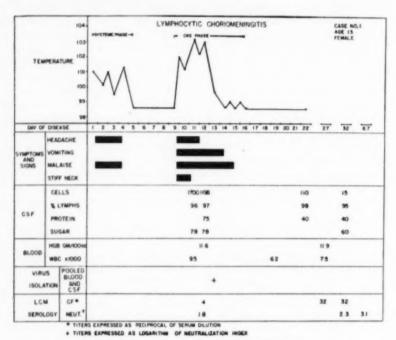


Fig. 1. Case 1: Lymphocytic choriomeningitis.

Clinical Laboratory Findings: The average white blood cell count on admission to the hospital in 63 of the proved cases of LCM was 8400 per cubic centimeter, with the differential count showing an average of 66 per cent of the cells to be of the polymorphonuclear type.

Table 5 presents the mean values of the cell counts and protein determinations in the spinal fluid in this series of cases. An average of 728 cells per cubic centimeter, principally lymphocytes, was found in the first four days of meningeal disease due to LCM. Although the counts ranged from 0 to 6,050, in only one instance was the value above 2,800. Thirty patients provided fluids during this period which had more than 600 cells, while 35 had less than this number. The cellular elements fell rapidly to an average value of 112 per cubic centimeter after the third week of illness. One patient

Table V
Cerebrospinal Fluid Values in 79 Cases of Lymphocytic Choriomeningitis

Day of Disease	Number of Specimens	Mean Value	Standard Deviation	Range
1-4	65	728	546	0-6050
5-7	28	564	398	2-2450
8-14 15-21	38	536	378 247	18-1700 0-1275

Day of Disease	Number of Specimens	Mean Value	Standard Deviation	Range
1-4	26	104	44	50-300
5-7	13	118	40	37-227
8-14	21	115	39	37-304
15-21	6	80	20	58-109
22+	9	71	33	15-163

who had a peak cell count of 700 on the third day of meningeal disease had only 13 cells on the forty-fourth day after onset of illness. Another with a peak count of 500 cells on the ninth day of disease still had 60 cells 32 days later.

In the latter half of the first week of meningeal disease a peak cerebrospinal fluid protein concentration of 118 mg, per 100 c.c. was demonstrated. The average protein level slowly fell to the still abnormal mean of 71 mg, per 100 c.c. by the fourth week of illness. In four cases in which cerebrospinal fluid proteins were determined 36 to 40 days after onset of the illness, levels of 35, 48, 112 and 163 mg, per 100 c.c. were found.

Figure 2 presents graphically the mean values for total cells and total protein in the spinal fluid at different periods of time after onset of meningitis in 79 patients suffering from infection by LCM virus. Included for comparison are the values encountered in the 86 cases of mumps meningitis discussed in the next section of this paper.

TABLE VI
Cerebrospinal Fluid Sugar Values in Laboratory Confirmed Cases of Lymphocytic Choriomeningitis, Mumps Meningitis, Herpes Simplex Meningitis and Leptospiral Meningitis

Disease	Number of Deter- minations	Over 70	50-70	Under 50	Lowest Value
LCM	72	17	36	19	17 mg. 9
Mumps Meningitis	76	23	46	7	17 mg. 9 27 mg.
Herpes Simplex Meningitis	6	2	3	1	110 (
Leptospiral Meningitis	8	2	5	1	40 mg.

Of considerable interest was the observation that 19 of 72 spinal fluids tested had levels of sugar below 50 mg. per 100 c.c. (table 6). The lowest spinal fluid sugar value observed was 17 mg. per cent, and seven other fluids had levels of 30 to 40 mg. per 100 c.c.

Virologic Findings: In this series of 79 cases of LCM, the complement-fixation test gave positive results in 69.6 per cent of the cases and negative

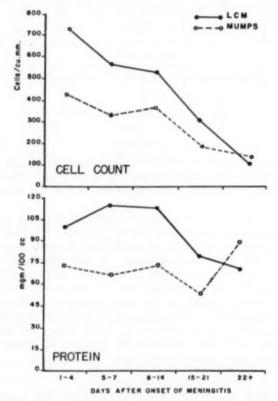


Fig. 2. Mean values in 79 cases of LCM and 86 cases of mumps meningitis according to days after onset of meningeal disease.

results in 29.1 per cent. The test was not done in 1.3 per cent of all cases. The neutralization test was positive in 86.1 per cent, negative in 5.1 per cent, and not done in 8.8 per cent of all cases. In 32 cases an attempt was made to isolate an infectious agent in laboratory animals; in 17 instances the results were positive, with identification of the agent as the virus of LCM. The virus was isolated in 12 of 24 attempts from spinal fluid and in 7 of 13 attempts from blood. There was some evidence that isolation

attempts were more often successful if the material was collected within the first six days of illness, although the virus was isolated as late as 16 days from spinal fluid and 17 days after the onset of meningeal disease from blood. There was no apparent correlation between the number of cells present in the spinal fluid specimens and the incidence of positive results in virus isolation attempts. In one instance LCM virus was recovered from a spinal fluid with only two cells per cubic centimeter, and in another instance an attempted isolation was negative in a case with 2,430 cells per cubic centimeter.

Figure 3 shows the average time of appearance of complement-fixing and neutralizing antibodies for LCM after the onset of meningeal disease. As has been shown by others, 17 complement-fixing antibodies rise to diagnostic levels in the third and fourth weeks of illness, persist at diagnostic

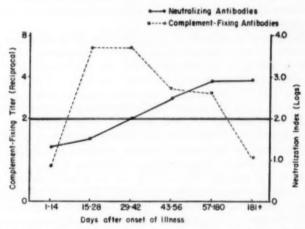


Fig. 3. Mean titer of complement-fixing and neutralizing antibodies in 70 odd cases of lymphocytic choriomeningitis by week of disease.

levels for a relatively short period of time, and are usually absent six months after the onset of the illness. On the other hand, neutralizing antibodies are much slower to appear, rising to diagnostic levels by the seventh and eighth weeks of illness and persisting at high levels for long periods of time. Sera collected seven to 11 months after the onset of illness in five of these cases still had high levels of neutralizing antibody. Neutralizing antibodies may persist for as long as four to five years after the acute illness.¹⁷

In six cases the neutralization test for LCM was positive in the first two weeks of illness, rendering the serologic diagnosis of LCM somewhat doubtful. However, the sera from four of these patients contained complement-fixing antibodies. Three of these four cases also showed a further rise of 10 or more LD₅₀ in the neutralization index and, in two instances,

the virus was recovered from the spinal fluid. In the other two cases, a further rise in the neutralization index of 13 and 100 LD50, respectively, when both sera were tested in the same protocol, was sufficient to confirm

the serologic diagnosis of LCM.

Of the 23 cases in which complement-fixing antibodies were not detected during the course of the illness, all showed a rise in neutralizing antibodies between acute and convalescent phases of illness. In two of these cases the virus was isolated from the spinal fluid. In both instances, specimens were taken at an optimal time after the acute illness for the detection of complement-fixing antibodies, although none was found. In only three of the 23 cases were the specimens taken at an improper time so that complement-fixing antibodies might not be expected to be present. In the remaining 20 cases, suitably timed specimens were tested and found negative, representing either a failure of the test to diagnose LCM in otherwise proved cases, or failure of the patient to produce detectable complement-fixing antibodies in response to his infection.

The divergence in antibody response of given patients when measured by the two technics was often marked. Thus, in 16 persons who developed neutralization indices of 3.6 logs or greater, the maximal complement-fixation titers were as follows: seven with 1:16; two with 1:4 to 1:8; one with 1:2; and six with 0. Similarly, in five other patients with a complement-fixation titer of 1:16, the neutralization indices were: three with values

of 2.5 to 3.5 logs; one with 2.0; and one of less than 1.3 logs.

Mumps Meningitis: Clinical Picture: The principal features of 86 cases of mumps infection of the central nervous system diagnosed by serologic procedures at the Army Medical Service Graduate School from 1941 to 1952 are shown in table 4. As in LCM, the three main findings are headache, fever and, to a lesser degree, stiff neck. The fever lasted an average of 7.3 days. Abnormal neurologic signs were noted in 20 (or 23.8 per cent) of the 86 cases. Seven patients had absent or hypoactive deep tendon reflexes, 10 had hyperactive reflexes, two presented a central type of unilateral facial paralysis, and one had a transient strabismus. Sixty-three and one-tenth per cent of the patients were fully alert and oriented throughout the illness, 23.7 per cent became drowsy and lethargic, 10.5 per cent were semicomatose, and 2.6 per cent were comatose. Vertigo was the only other common symptom of central nervous system disease during mumps infection. Of the 11 patients with signs of respiratory disease, five presented coughs and three had x-ray evidence of pneumonitis. Twelve patients complained of epigastric abdominal pain, but in none was there confirmatory evidence of pancreatitis.

Only 50.6 per cent of the patients studied in this series of cases had evidence of parotitis at some time during the course of their illness; 23.7 per cent had an associated orchitis; 54.8 per cent had either parotitis or orchitis in addition to the meningitis (table 7). Thus, 45.2 per cent of the cases had meningeal signs only, without other evidence of mumps infection.

The onset of meningitis was prior to the appearance of parotitis in the majority of cases in the present group. Fifty-two and five-tenths per cent of 40 patients with both meningitis and parotitis had evidence of meningitis on an average of 5.6 days prior to the onset of parotid swelling. In 7.5 per cent of the cases the meningitis occurred concomitant with the parotitis, and in 40 per cent of the cases it occurred an average of 4.4 days after the onset of parotitis. The appearance of meningitis prior to the appearance of parotitis in the majority of patients in this series is in contrast to other well studied series of mumps meningitis 18, 19, 20, 21, 22 in which meningitis has been shown to occur on the average of two to 10 days after the onset of parotitis. An obvious explanation for the difference lies in the selection of the cases. At the onset of illness these cases were considered to be aseptic meningitis and, as such, were presented to the laboratory for serologic

TABLE VII

Relation of Meningitis to Other Manifestations of Mumps in Laboratory Confirmed Cases of Mumps Meningitis, Army Medical Service Graduate School, 1941-1952

	Nu	mber	Per	Average
	Total*	Positive	Cent	Day
A. Manifestations of Mumps Infection				
1. Meningitis Alone	84	38	45.2	-
2. Meningitis and Parotitis	79 76	40	50.6	
3. Meningitis and Orchitis		18	23.7	-
4. Meningitis with Parotitis or Orchitis	84	46	54.8	-
B. Relation of Onset of Meningitis to Onset of Parotitis				
1. Meningitis Prior to Parotitis	40	21	52.5	5.6
2. Meningitis Concomitant with Parotitis	40	3	7.5	
3. Meningitis Subsequent to Parotitis	40	16	40.0	4.4

^{*} Number with sufficient data to interpret.

studies. Those cases with parotitis apparent at or prior to the onset of meningitis usually would not be considered as diagnostic problems, and thus often would not be referred to this laboratory for serologic confirmation, the clinical diagnosis being sufficiently precise.

Complications and residuals of this disease were few. One adult presented a weakness of the right leg, thickness of speech, blindness of the left eye and a left facial paralysis in the course of the acute illness, with slow recovery. Another had clonic and tonic convulsions, spasticity, nystagmus and dysphagia in the acute phase of the illness. A third presented hyperactivity, purposeless movements and psychotic delusions for a six day period. Two others presented evidence of myocarditis. In one case an electrocardiogram taken on admission to the hospital (seven days after the onset of parotitis) was normal, but six days later showed inverted TV₁, TV₂ and

An electrocardiogram taken shortly prior to death five days later showed evidence of an atrioventricular block. This 30 year old male, the only fatal case of mumps meningitis in the series, developed orchitis and signs of meningitis 14 days after exposure to a brother with parotitis and three days before the onset of his parotitis. Seven days later, after apparent recovery from the parotitis and orchitis, he developed a pulmonary infarct and subsequently died. Microscopic examination of the heart revealed evidence of interstitial edema, fibrin deposition, particularly in the auricular myocardium, swelling of the myocytes and minimal patchy infiltrations of lymphocytes, eosinophils and large mononuclear cells throughout the myocardium. In addition to the myocarditis there were multiple pulmonary Small mononuclear leukocytes were seen scattered through the The electrocardiographic findings in the other case were tran-Ten days after the onset of his illness, and in the absence of clinical evidence of myocarditis, an electrocardiogram showed a diphasic T₁, and inverted TCF4 and TCF5. Conduction time and heart rate were normal and the rhythm was regular. Three days later T1, TCF4 and TCF5 were upright and the electrocardiogram was normal. Subsequent electrocardiograms 17 and 34 days after onset of the illness were also essentially normal. Following is an abstract of the illness in one of the cases of mumps meningitis in this series.

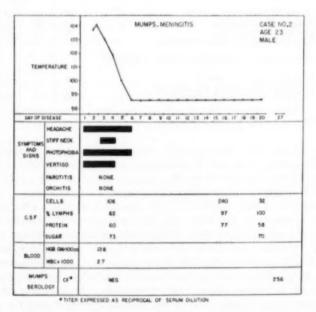


Fig. 4. Case 2: Mumps meningitis without parotitis or orchitis.

TABLE VIII
Cerebrospinal Fluid Values in 86 Cases of Mumps Meningitis

1-4 58	410	228	9-1696
5-7 34	330	120	2-1028
8-14 30	366	310	1-1620

	****	tem (mg. per roo	,	
Day of Disease	Number of Specimens	Mean Value	Standard Deviation	Range
1-4	31	74	27	20-250
5-7	14	68	22	22-180
8-14	20	74	26	20-290
15-21	6	53	23	30-77
22+	4	90	66	28-224

Case 2. A 23 year old white male was admitted to a Veterans Administration Hospital on May 11, 1951, with the chief complaint of severe headache and fever. On awakening on May 10 he had noted a severe throbbing bitemporal headache, photophobia and dizziness. Six hours later he had a severe chill with high fever. On admission to the hospital his temperature was 103.4° F., and he appeared acutely ill. Physical examination was essentially negative, with no abnormal neurologic findings noted. A clinical diagnosis of tularemia was made and therapy with streptomycin was instituted on May 12, at which time the temperature was 103° F. A stiff neck was first noted on the same day. A spinal tap done on May 13 showed: 106 cells per cubic centimeter, 62 per cent of which were lymphocytes; protein, 60 mg. per 100 c.c.; sugar, 73 mg. per 100 c.c.; negative smear and sterile culture. The fever dropped by rapid lysis to normal by May 15, after which time the patient was afebrile and asymptomatic. The stiff neck disappeared on May 13. No skin rash, no parotitis, no orchitis and no abnormal neurologic findings were noted. Subsequent spinal fluid findings are shown in figure 4. Other laboratory studies were as follows: white blood cell count, 2,700 cells per cubic centimeter; differential count: 79 per cent segmented forms, 19 per cent lymphocytes and 2 per cent monocytes; urine, negative; blood and urine cultures, sterile. Agglutination tests for typhoid, paratyphoid, brucellosis and tularemia were negative on May 11 and May 24. Complement-fixation tests for mumps were negative on May 13 and positive at a titer of 1:256 on June 6.

Clinical Laboratory Findings: The average white blood cell count in this series of cases of mumps meningitis was 9,070 per cubic centimeter, with an average differential count of 64 per cent polymorphonuclear leukocytes.

The mean spinal fluid values for cases of mumps meningitis are listed in table 8 and diagrammed in figure 2. The mean count of 410 cells per cubic centimeter found in the first four days of illness was significantly lower than the average cell count for LCM in the same time period. In addition, the range of cell counts was narrower in the cases of mumps meningitis,

with a maximal count of 1,696 cells per cubic centimeter observed in one case. The cerebrospinal fluid protein value persisted at abnormal levels for a considerable period of time, as shown in figure 2. The spinal fluid sugar was below 50 mg. per 100 c.c. in seven of 76 instances in which it was tested (table 6). The lowest value observed was 27 mg. per 100 c.c.

Virologic Findings: Eighty-five cases in this series were selected as mumps meningitis on the basis of serologic evidence of recent mumps infection, using the complement-fixation technic with a parotid antigen. In one additional case a diagnosis of mumps meningitis was established by the isolation of the virus from a specimen of spinal fluid collected on the second day of illness. It has been the experience of this laboratory and others 22 that this complement-fixation technic is highly specific in the diagnosis of mumps parotitis. It is probable, therefore, that only an insignificant number, if any, of the complement-fixation tests performed were either falsely negative or falsely positive for mumps. The sera of 61 of the cases of mumps meningitis were also tested and found negative in complement-fixation tests for LCM: two were found to be negative on complementfixation tests with the antigen common to the psittacosis-lymphogranuloma venereum group of viruses; three were negative for Western equine encephalomyelitis, and one was negative for Eastern equine encephalomyelitis by complement-fixation tests.

Herpes Meningitis: Clinical Picture: The six * cases of herpes simplex meningitis reported in this study apparently represented primary infections with the virus of herpes simplex, since the patients did not possess neutralizing antibodies against herpes simplex virus at the onset of their acute infection but developed them during convalescence. If cases of recurrent herpes simplex meningitis do occur,25 it has not been possible to prove their etiology with the technics employed in the present work. All six of the present cases presented a moderately severe illness (table 4). All had fever and headache; five had nuchal rigidity. The acute illness was prolonged, as indicated by an average febrile period of 13 days. Nausea and vomiting, malaise, weakness, aches and pains were common. In four of the six patients there were abnormal neurologic signs, and in three manifestations of acute central nervous system disease were moderately severe. One patient had diplopia, dysarthria and nystagmus. One had convulsions and a marked memory defect. One had urinary incontinence and also developed respiratory paralysis, necessitating artificial respiration by means of a mechanical respirator; however, he recovered rapidly without residual paralysis. The only neurologic abnormality noted in one other patient was hyperactivity of the deep tendon reflexes. Indicative also of the relative severity of this disease was the presence of lethargy and stupor in three of the six patients. One patient had mild vertigo, none had signs of respiratory disease, conjunctivitis, abdominal pain, backache or muco-

^{*} Five of these cases have also been mentioned by Afzelius-Alm.24

cutaneous herpes. Following is an abstract of one of the cases of herpes simplex meningitis in this series.

Case 3. A 21 year old white male was admitted to an Army Hospital on August 6, 1949. He had first become ill on July 30, with headache, malaise and a fever of 102.4° F., followed on July 31 by vomiting. On August 3 he felt well and was afebrile, but on August 4 the symptoms recurred with a severe headache, nausea and vomiting. Physical examination showed a lethargic, acutely ill patient with a temperature of 101° F. and marked nuchal rigidity. Otherwise the neurologic examination was entirely normal except for some diminution on both knee jerks. The white blood cell count on August 6 was 9,300 cells per cubic centimeter, 75 per cent of which were polymorphonuclear leukocytes. A spinal tap on August 6, at the time of admission to the hospital, showed 306 cells per cubic centimeter, 46 per cent of which were lymphocytes. By August 8 he was feeling well and by August 12 was asymptomatic, with no nuchal rigidity. Subsequent spinal fluid findings are shown in figure 5. Serum collected on August 9, August 29 and September 13 were negative for complement-fixing antibodies of LCM and mumps. Neutralization tests for St. Louis encephalitis and Western equine encephalomyelitis on the sera collected on August 9 and August 29 were negative, as were neutralization tests for LCM performed on sera collected September 13 and November 8. Sera drawn August 9, the eleventh day of illness, did not neutralize herpes simplex virus in a neutralization test employing the chorioallantoic membrane of embryonated eggs, whereas the serum collected on August 31, 33 days after onset of the illness, did neutralize herpes simplex virus. These neutralization results were confirmed on two subsequent occasions.

Clinical Laboratory Findings: The average white blood cell count in these cases of herpes simplex meningitis was 9,260 cells per cubic centi-

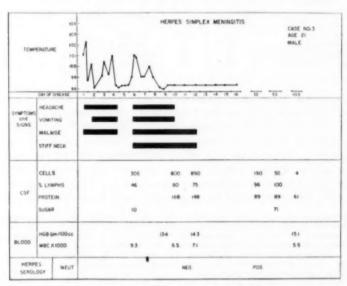


Fig. 5. Case 3: Herpes simplex meningitis.

meter, with an average differential count of 64 per cent polymorphonuclear leukocytes. In the first seven days of illness the mean cerebrospinal fluid cell count was 240 cells per cubic centimeter, and the mean protein, 66 mg. per 100 c.c. (table 9). Insufficient determinations were available in this small group of cases to calculate mean values for the cell count and protein by the week of disease, as was done for LCM and mumps meningitis. One patient had an abnormally low cerebrospinal fluid sugar of 10 mg. per 100 c.c. in the acute phase of the illness (table 6), but in the other cases the cerebrospinal fluid sugar was within normal limits.

Virologic Findings: The six cases of herpes simplex meningitis * in this series were selected on the basis of serologic evidence of primary herpetic infection. The results of the neutralization tests were confirmed in three instances by the use of the complement-fixation technic. 26 In two cases complement-fixing antibodies were present at the same titer in both acute and convalescent phase sera; in one instance no complement-fixing antibodies could be demonstrated in specimens of serum drawn 12 and 23 days after onset of illness.

TABLE IX

Comparative Cerebrospinal Fluid Values in Laboratory Confirmed Cases of Lymphocytic Choriomeningitis, Mumps Meningitis, Herpes Simplex Meningitis and Leptospiral Meningitis in First Seven Days of Illness

Disease	Cell Count (per cubic centimeter)			Protein (mg. per 100 c.c.)		
	Number of Specimena	Mean Value	Range	Number of Specimens	Mean Value	Range
LCM	65	678	0-6050	26	112	37-300
Mumps Meningitis	58	378	2-1696	31	72	20-250
Herpes Simplex Meningitis	9	240	100-400	3	66	39-120
Leptospiral Meningitis	10	334	32-1000	5	65	42-80

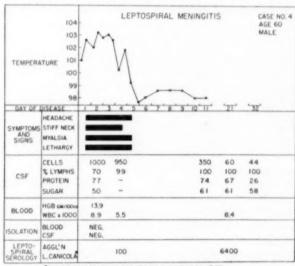
Leptospiral Meningitis: Clinical Picture: The findings in 12 cases † of leptospiral meningitis are listed in table 4. Fever was the feature common to all. Eleven had headache and 10 presented a stiff neck. The acute phase of disease, as indicated by the duration of fever, lasted an average of 7.9 days and was often accompanied by nausea, vomiting, malaise and weakness. One of the two patients with abnormal neurologic findings had a transient weakness of the right leg and a hypoactive right ankle jerk; the other patient had hyperactive deep tendon reflexes. In four

† One of these cases has been presented by Coffey et al.27; another was mentioned by Beeson and Hankey.28

^{*}Subsequent to this study two additional cases of herpes simplex meningitis have been detected in this laboratory during serologic studies on cases of aseptic meningitis. In one instance the serologic diagnosis was established by a significant increase in both neutralizing and complement-fixing antibodies. In the other case, a sixteenfold or greater increase in complement-fixing antibodies was demonstrated during convalescence from an acute central nervous system infection; neutralizing antibodies were present in the same acute and convalescent phase sera.

instances there was pleuritic chest pain; indeed, in one patient with hemoptysis, pneumonitis of the right lower lobe was demonstrated by roentgen examination. In all but one instance the patients were fully alert and oriented. There were no complications or serious residual damage noted in any of this small group of cases. Following is a brief account of a case of leptospiral meningitis studied in this series.

Case 4. A 60 year old retired veterinary officer was admitted to an Army Hospital on January 22, 1952, for urologic studies. On January 25 his temperature rose from normal levels to 102.6° F., and he noted a severe frontal headache, anorexia, mild generalized aches and pains, malaise and lethargy. Physical examination at this time was negative except for a moderately stiff neck. From January 8 to January 14 he had been hospitalized elsewhere because of an acute illness with pain in the chest and the low back, chills, fever, headache and a nonproductive cough. At that time a white blood count was 7,300, with a normal differential; a chest x-ray was normal. Recovery from this episode was prompt, although the patient continued to complain of right flank pain. Pertinent laboratory findings on January 26 were: white blood count, 8,900 cells per cubic centimeter; differential count: 51 per cent neutrophils, 40 per cent lymphocytes, 7 per cent monocytes and 2 per cent eosinophils; urine, normal; blood culture and malaria smear on January 26 were negative; chest x-ray on January 27 was normal. Cerebrospinal fluid on January 26: cells, 1,000, of which 70 per cent were lymphocytes, and 30 per cent were polymorphonuclear leukocytes; protein, 77 mg. per 100 c.c.; sugar, 50 mg. per 100 c.c.; chlorides, 110 mEq. per L.; and colloidal gold, 1122210000. Subsequent spinal fluid findings are shown in figure 6. Attempts to isolate an infectious agent, including leptospires, from spinal fluid and blood collected on



*TITERS EXPRESSED AS RECIPROCAL OF SERUM DILUTION

Fig. 6. Case 4: Leptospiral meningitis due to L. canicola.

January 28, 1952 gave negative results. Agglutinins for Leptospira canicola increased from a titer of 1:100 in serum drawn on the fourth day of illness to a titer of 1:6,400 in serum drawn 21 days after onset of illness. Sera drawn 4, 14, 21 and 39 days after the onset of illness were negative for complement-fixing antibodies of LCM; 4 day and 21 day sera were negative for complement-fixing antibodies of mumps, and 4 and 39 day sera were negative for neutralizing antibodies of LCM.

Clinical Laboratory Findings: The average white blood cell count in these cases of leptospiral meningitis was 9,610 cells per cubic centimeter, of which 72 per cent were of the polymorphonuclear type. The mean cerebrospinal fluid cell count and protein in the first seven days of illness were 334 cells per cubic centimeter and 65 mg. per 100 c.c., respectively (table 9). Again, insufficient cell counts and protein values were available in this group of cases to calculate mean values by week of illness. The highest cell count recorded was 1000 cells per cubic centimeter, and the lowest, 32 cells per cubic centimeter. In one instance a spinal fluid sugar of 40 mg. per 100 c.c. was found (table 6).

Leptospiral Findings: The 12 cases of leptospiral meningitis in this series were selected on the basis of serologic evidence of recent leptospiral infection. Technics for the isolation of leptospires were not part of the routine diagnostic isolation procedure in cases of acute central nervous system disease during the period of this study, so that in none of these 12 cases were leptospires isolated from the spinal fluid. On the basis of leptospiral agglutination tests, the serogroups involved in these cases were as follows: pomona, four cases; canicola, five cases; ballum, one case;

bataviae S, one case; and grippotyphosa, one case.

DISCUSSION

The cases of aseptic meningitis for whom no etiologic diagnosis was established and which constituted about three quarters of the total group require further study. No doubt some of these represent cases of nonparalytic poliomyelitis which occur in and out of the epidemic poliomyelitis season. The determination of the exact incidence of poliomyelitis in the etiology of aseptic meningitis, however, must await the development and standardization of the newer tools available for the serologic diagnosis of poliomyelitis, i.e., the complement-fixation test 29 and tissue culture neutralization technics.30 Other agents that have been shown to produce acute aseptic meningitis, in the absence of the more common manifestations of the illnesses, are the viruses of lymphogranuloma venereum,31 infectious mononucleosis,32 infectious lymphocytosis,33 the Coxsackie group of viruses 34 and the arthropod-borne encephalitides (Western and Eastern equine encephalomyelitis, St. Louis encephalitis).4 Diseases of the human central nervous system due to viruses of the encephalomyocarditis, Colombia-SK, MM, and Mengo group have been described 35, 36; it would appear, however, that viruses of this group rarely infect man.37 The neurotropic viruses isolated from mosquitoes in Africa and South America and studied by Smithburn ^{as} are of general interest in the field of neurotropic virus disease but, due to their restricted geographic distribution, they have not been studied in relation to the present group of cases. The rôle of the California virus, ^{as} Verlinde virus ⁴⁰ and the viruses of primary atypical pneumonia, infectious hepatitis and Colorado tick fever in the causation of acute nonbacterial meningitis has not been adequately assessed. Whether cases which belong in the group of demyelinating encephalitides, ⁴¹ viz., postinfectious and postvaccinal encephalitis and multiple sclerosis, ever present, in their milder forms, findings suggestive of aseptic meningitis remains to be determined.

It has been claimed ⁴² that certain cases of aseptic meningitis may be allergic in nature and attributable to some of the common pathogenic microorganisms inducing disease in the oropharynx. In addition to the causes mentioned above, Nordwall ⁴³ lists the following as occasionally producing a clinical picture similar to aseptic meningitis: meningitis secondary to local inflammation, meningitis due to sepsis (metastatic), herpes zoster, lues, trauma, sun exposure or sunstroke, medicaments (drugs), lead intoxication, helminthiasis, tumor (cancer), uremia and meningeal bleeding. Toxoplasmosis, ⁴⁴ torulosis ⁴⁶ and acute syphilitic meningitis ⁴⁶ must also be considered in the differential diagnosis in certain patients acutely ill

with a nonbacterial meningitis.

The clinical features of infection with any one of the four agents studied intensively in the present investigation are quite similar. Nearly all of the cases presented the triad of fever, headache and stiff neck, along with various associated symptoms and signs of minor importance. The severity of the illnesses may be judged by the total duration of fever and the degree of change in the sensorium of these patients. In the study of lymphocytic choriomeningitis, mumps meningitis and leptospiral meningitis, the length of the febrile period was shown to be 5.8, 7.3 and 7.9 days, respectively. Similarly, 70.2 per cent, 63.1 per cent and 91.6 per cent, respectively, of the cases of LCM, mumps meningitis and leptospiral meningitis were fully alert and oriented throughout the course of their acute illness. However, the findings in the cases of herpes simplex meningitis are somewhat different. Thus, the fever lasted an average of 13 days (six, seven, nine, 17 and 26 days in five of the six cases); and three of the six cases were lethargic or slightly stuporous during the course of their illness. Another indication of the increased severity of disease in patients with herpes simplex meningitis is the presence of abnormal findings on neurologic examination in four of the six cases. However, the series of six cases is small in comparison with the larger series of LCM and mumps meningitis; hence, definite conclusions are not warranted. Worthy of note, in passing, is the absence of any cutaneous manifestation of herpes simplex infection in the six cases of primary herpes simplex meningitis.

Contrary to the popular belief,47 the spinal fluid sugar may be abnormally low in cases of LCM.48 Although there was no simultaneous testing of the blood sugar in these cases, 26 per cent of the spinal fluid sugar values in LCM, 9.2 per cent in mumps meningitis, 17 per cent in herpes simplex meningitis and 12.5 per cent in leptospiral meningitis were lower than might be expected without clinically evident hypoglycemia (table 6). In a retrospective study such as this, one should avoid any dogmatic statement regarding these findings in the absence of knowledge of the promptness with which the sugar content was determined after collection of the spinal fluid specimen. Nevertheless, assuming that the incidence of falsely low sugar determinations should be the same in series of cases of comparable size, the difference between the incidence of abnormally low spinal fluid sugar in cases of LCM (19 in 72) and mumps (7 in 76) might be expected to occur by chance only once in 140 times (P = .007). Therefore, it would appear justified to assume that the occurrence of abnormally low spinal fluid sugar values is characteristic of a proportion of cases of LCM.

The spinal fluid cell count may be of considerable aid in differentiating cases of aseptic meningitis. Cell counts of 50 to 200 are commonly seen in poliomyelitis, but rarely is the cell count in this disease over 500.⁴⁹ On the other hand, cell counts in the bacterial meningitides are usually over 1,000 cells per cubic centimeter, and most often of the polymorphonuclear variety.⁵⁰ Whereas cell counts in the 650 to 1,500 per cubic centimeter range may be due to other agents, if they are predominantly of the lymphocytic type LCM must be seriously considered. Cell counts in the 250 to 500 per cubic centimeter range, on the other hand, are difficult to interpret. In many of the cases of LCM in this series the cell counts fell within this range, as did most of the cases of mumps meningitis. Although the mean cell counts in herpes simplex meningitis and leptospiral meningitis are lower than those in mumps meningitis and LCM, the difference is insufficient to be of value in the differential diagnosis of these diseases (table 8).

Several findings are of interest in the series of 79 cases of LCM. One is the absence of evident pneumonitis in any of the cases studied. That this agent can produce pneumonitis in the infected guinea pig 3, 51 and monkey 3, 52 is well known. Indeed, certain cases of human LCM infections have been associated with a pneumonitis. 16, 55, 54 In one instance 54 the virus was isolated from the consolidated lung of a fatal case of systemic LCM in which there was no evidence of meningeal disease.

The relative low incidence of any paralytic manifestations in patients with LCM is the common experience; however, two of our 79 displayed such phenomena, as did a few of the British cases. 55, 56 Our two patients who exhibited muscle paralysis subsequently died. In the majority of instances recovery from acute LCM was uncomplicated, without relapse and without sequelae. The development of Parkinsonism noted in two

of the cases in this series is unusual; whether the manifestations of Parkinsonism were related to the acute central nervous system illness diagnosed as LCM or due to some other etiologic factor cannot be stated. None of the patients in this series developed blockage of the spinal fluid drainage

system, as has been reported by others. 87, 58

The clinical and laboratory features of mumps infection have been well documented elsewhere. 18, 19, 20, 21, 22 In most instances in the present group of cases the disease was of the uncomplicated aseptic meningitis type. Three cases, however, presented findings of the encephalitic form of mumps infection. In one instance muscle weakness, dysarthria and transient blindness were observed; in another, there were choreiform movements, motor signs of an upper motor neurone lesion, and mental delusions; in the third there were convulsions, nystagmus, dysphagia and spasticity. In no instance was there myelitis, neuritis or any of the rarer manifestations of mumps central nervous system disease. 18

The two cases of mumps myocarditis occurring in this series are of interest. Wendkos and Noll ⁶⁹ were the first to describe electrocardiographic changes indicative of myocarditis in cases of mumps. Rosenberg ⁶⁰ demonstrated transient electrocardiographic changes in 15.4 per cent of 104 patients with epidemic parotitis, and showed that the changes usually occurred five to 10 days after onset of the mumps. In one of our patients the myocarditis was first evident 13 days after the onset of the parotitis and six days after the first pulmonary infarct. While the electrocardiographic changes in this particular patient could have resulted from the pulmonary infarction, the histopathologic lesions found in the myocardium were probably the result of the recent mumps infection. In the other case, electrocardiographic evidence of myocarditis was encountered on the tenth day of illness, but these abnormalities had disappeared by the thirteenth day.

Orchitis occurred in 18 of the 76 males ill with mumps meningitis. There was no evident relationship between the onset of the orchitis and the onset of parotitis or meningitis. In six of the cases meningitis and orchitis occurred in the absence of parotitis. It was not possible to evaluate

the incidence of pancreatitis in this series of cases.

The seasonal incidence of LCM and mumps meningitis is shown in figure 7. There is a sharp rise in the incidence of LCM in the late fall, to a peak incidence in December; thereafter, the number of cases decreases to a fairly constant level during the winter and spring months. A seasonal decline is noted in the summer to a low in the month of August. A similar seasonal incidence for LCM was noted by Armstrong, 11 who related the relative infrequency of LCM in the summer months to the migration of house mice into the fields during warm weather, and the rise in incidence in September, October, November and December to their return to the house at the onset of colder weather. The graph for mumps meningitis closely follows the seasonal curve of incidence of mumps parotitis. 12 There is a sharp rise in

incidence in February and early spring from a seasonal low in late fall and early winter.

The clinical findings in the cases of leptospiral meningitis are essentially similar to those present in lymphocytic choriomeningitis and mumps meningitis. Headache, stiff neck and fever were the most common features. Myalgia and malaise, when present, were prominent symptoms. Conjunctival injection or suffusion was not mentioned as occurring in the majority of patients in this series. In no instance was there evidence of significant hepatic involvement in this series of cases. There were no sequelae reported and no deaths. In four of the patients, possible exposure to leptospirosis in lower animals was recorded. One patient had assisted in the vaccination of cows at his father-in-law's farm for two to three weeks before admission.

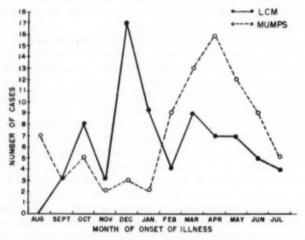


Fig. 7. Seasonal incidence of lymphocytic choriomeningitis and mumps meningitis.

The cows were said to have "tick fever." In this same time period he had also killed and disposed of many rats. The causative organism in his illness was Leptospira pomona, which is widespread among swine and cattle in the United States. A second patient had drunk river water while on a fishing trip three weeks prior to onset of his illness; the causative organism in this case was Lept. grippotyphosa. The third patient had been working on a farm with sick hogs and two weeks prior to the start of his illness had extracted a placenta from a cow, although the cow was apparently well. In this instance the agent was Lept. pomona. The fourth patient (case 4) was a retired veterinary officer in practice in Delaware, where he had treated many sick dogs within the month prior to onset of his central nervous system illness. Lept. canicola was the infecting organism in this instance. Ten of the cases occurred in southern states: Texas, three; Louisiana, three;

Tennessee, three, and Virginia, one. The other cases occurred in Delaware and Iowa. This series of cases is too small to determine the true seasonal incidence; cases occurred in every month of the year except May, June, July and December.

The incidences of infection with the agents of LCM, mumps, herpes simplex and leptospirosis in the present group of sporadic cases of acute aseptic meningitis may be considered as reasonably typical of those which might be encountered in other large groups of such cases among military personnel and their dependents, and veterans within the continental limits of the United States. The distribution of infections with these four agents in series of cases of aseptic meningitis studied by other authors 28, 64, 65, 66 is in general agreement with the present findings. However, some variation in the incidence is to be anticipated, since there are differences in the methods of selection employed, the population groups studied and other factors. This is well illustrated by the incidence of mumps infection in the groups of cases of aseptic meningitis studied by Enders 67 and by ourselves. He found that mumps infection accounted for approximately two-thirds of 51 cases of aseptic meningitis encountered in pediatric practice in Boston. In general terms, it may be stated that the viruses of LCM and mumps are each responsible for about 10 per cent of the cases of aseptic meningitis, and that the virus of herpes simplex and the leptospires are together responsible for another 10 per cent of these cases. The possible rôle of other known viruses in the etiology of the cases which now remain undiagnosed has already been discussed. In the present era of widespread administration of antibiotics, which are often given at the onset of a febrile illness prior to the establishment of a specific diagnosis, one must also consider the rôle of controlled bacterial infection in the syndrome of aseptic meningitis.

SUMMARY

Eight hundred fifty-four sporadic cases of acute aseptic meningitis occurring among military and veteran personnel and their dependents in the continental United States in the 11 year period 1941–1952 have been reviewed. Approximately 9 per cent of these cases were caused by infection with LCM virus and 12 per cent with mumps virus. Studies since 1950 on a portion of the patients in this series indicate that the virus of herpes simplex was responsible for about 5 per cent and the leptospires for about 7 per cent of these selected cases.

The clinical and laboratory features of each of these specific illnesses

have been presented.

No specific etiologic agent was incriminated in approximately threequarters of the cases of sporadic aseptic meningitis studied. The application of newly developed diagnostic procedures and the more extensive use of available diagnostic technics may be expected to reduce the size of this undiagnosed group.

BIBLIOGRAPHY

- Wallgren, A.: Une nouvelle maladie infectieuse due système nerveux central? Acta pædiat. 4: 158, 1925.
- Smadel, J. E., and Adair, C. V.: Laboratory aspects of the differential diagnosis in acute poliomyelitis. Poliomyelitis: papers and discussions presented at the Second International Poliomyelitis Conference, 1952, J. B. Lippincott, Philadelphia, p. 164.
- Smadel, J. E., Baird, R. D., and Wall, M. J.: A soluble antigen of lymphocytic choriomeningitis. I. Separation of soluble antigen from virus, J. Exper. Med. 70: 53, 1939.
- Hammon, W. M.: Encephalitis (arthropod-borne virus encephalitides and lymphocytic choriomeningitis): chapter in Diagnostic procedures for virus and rickettsial diseases, 1948, American Public Health Association, New York, p. 187.
- Rogers, N. G.: The effect of Merthiolate on the infectivity of certain viruses, J. Lab. and Clin. Med. 38: 483, 1951.
- Smadel, J. E., and Wall, M. J.: Identification of the virus of lymphocytic choriomeningitis, J. Bact. 41: 421, 1941.
- Enders, J. F., and Cohen, S.: Detection of antibody by complement-fixation in sera of man and monkey convalescent from mumps, Proc. Soc. Exper. Biol. and Med. 50: 180, 1942.
- Habel, K.: Cultivation of mumps virus in the developing chick embryo and its application to studies of immunity to mumps in man, Pub. Health Rep. 60: 201, 1945.
- Levens, J. H., and Enders, J. F.: The hemoagglutinative properties of amniotic fluid from embryonated eggs infected with mumps virus, Science 102: 117, 1945.
- Burnet, F. M., and Lush, D.: The inactivation of herpes virus by immune sera: experiments using the chorio-allantoic membrane technique, J. Path. and Bact. 48: 275, 1939.
- Burnet, F. M., and Williams, S. W.: Herpes simplex: a new point of view, M. J. Australia 1: 637, 1939.
- Schüffner, W., and Mochtar, A.: Versuche zur Aufteilung von Leptospirenstämmen, mit einleitenden Bemerkungen über den Verlauf von Agglutination und Lysis, Zentralbl. f. Bakt. 101: 405, 1927.
- Gochenour, W. S., Jr., Yager, R. H., Wetmore, P. W., and Hightower, J. A.: Laboratory diagnosis of leptospirosis, Am. J. Pub. Health 43: 405-410, 1953.
- Rasmussen, A. F.: The laboratory diagnosis of lymphocytic choriomeningitis and mumps, Rocky Mountain Conference on Infantile Paralysis, 1946, University of Colorado School of Medicine and Hospitals, Denver, p. 45.
- Havens, W. P., Jr.: Lymphocytic choriomeningitis—report of a case occurring in a granary harboring infected mice, J. A. M. A. 137: 857, 1948.
- Lépine, P., Mollaret, P., and Kreis, G.: Réceptivité de l'homme au virus murin de la chorioméningite lymphocytaire. Reproduction expérimentale de la meningite lymphocytaire bénigne, Compt. rend. Acad. d. sc. 204: 1846, 1937.
- Smadel, J. E., and Wall, M. J.: A soluble antigen of lymphocytic choriomeningitis.
 III. Independence of anti-soluble substance antibodies and neutralizing antibodies, and the rôle of soluble antigen and inactive virus in immunity to infection, J. Exper. Med. 72: 389, 1940.
- Bang, H. O., and Bang, J.: Involvement of central nervous system in mumps, Acta med. Scandinav. 113: 487, 1943.
- 19. Silver, H.: Meningitis in mumps, Acta med. Scandinav. 88: 355, 1936.
- Levison, H., and Thordarson, O.: Mumps meningitis and meningo-encephalitis, Acta med. Scandinav. 112: 314, 1942.
- 21. Steinberg, C. L.: Mumps meningo-encephalitis, U. S. Nav. M. Bull. 42: 567, 1944.
- Fox, M. J., and Grotts, B. F.: Central nervous system involvement in parotitis, J. Pediat. 35: 561, 1949.

- Enders, J. F., Cohen, S., and Kane, L. W.: Immunity in mumps. II. The development of complement-fixing antibody and dermal hypersensitivity in human beings following mumps, J. Exper. Med. 81: 119, 1945.
- Afzelius-Alm, L.: Aseptic encephalomeningitides in Gothenburg 1932-1950, Acta med. Scandinav. Suppl. 263: 1951.
- Janbon, M., Chaptal, J., and Labraque-Bordenave, M.: Le problème de la méningite herpétique. Contribution a son étude clinique et expérimentale, Presse méd. 50: 145, 1942.
- Gajdusek, D. C., Robbins, M. L., and Robbins, F. C.: Diagnosis of herpes simplex infections by the complement-fixation test, J. A. M. A. 149: 235, 1952.
- Coffey, J. H., Dravin, I., and Dine, W. C.: Swineherd's disease (aseptic meningitis) due to Leptospira pomona, J. A. M. A. 147: 949, 1951.
- Beeson, P. B., and Hankey, D. D.: Leptospiral meningitis, Arch. Int. Med. 89: 575, 1952.
- Casals, J., Olitsky, P. K., and Anslow, R. O.: A specific complement-fixation test for infection with poliomyelitis virus, J. Exper. Med. 94: 123, 1951.
- Robbins, F. C., Enders, J. F., Weller, T. H., and Florentino, G. L.: Studies on the cultivation of poliomyelitis viruses in tissue culture. V. The direct isolation and sero-logic identification of virus strains in tissue culture from patients with non-paralytic and paralytic poliomyelitis, Am. J. Hyg. 54: 286, 1951.
- Sabin, A. B., and Aring, C. D.: Meningo-encephalitis in man caused by the virus of lymphogranuloma venereum, J. A. M. A. 120: 1376, 1942.
- Bernstein, T. C., and Wolff, H. G.: Involvement of the nervous system in infectious mononucleosis, Ann. Int. Med. 33: 1120, 1950.
- Beloff, J. S., and Gang, K. M.: Acute poliomyelitis and acute infectious lymphocytosis.
 Their apparent simultaneous occurrence in a summer camp, J. Pediat. 26: 586, 1945.
- Shaw, E. W., Melnick, J. L., and Curnen, E. C.: Infection of laboratory workers with Coxsackie viruses, Ann. Int. Med. 33: 32, 1950.
- Smadel, J. E., and Warren, J.: The virus of encephalomyocarditis and its apparent causation of disease in man, J. Clin. Investigation 26: 1197, 1947.
- Dick, G. W. A., Best, A. M., Haddow, A. J., and Smithburn, K. C.: Mengo encephalomyelitis. A hitherto unknown virus affecting man, Lancet 2: 286, 1948.
- Warren, J., Smadel, J. E., and Russ, S. B.: The family relationship of encephalomyocarditis, Columbia-SK, MM, and Mengo encephalomyelitis viruses, J. Immunol. 62: 387, 1949.
- Smithburn, K. C.: Studies on certain viruses isolated in the tropics of Africa and South America. Immunological reactions as determined by cross-neutralization tests, J. Immunol. 68: 441, 1952.
- Hammon, W. McD., and Reeves, W. C.: California encephalitis virus. A newly described agent, California Med. 77: 303, 1952.
- Verlinde, J. D., van der Werff, J., and Briët, W., Jr.: An encephalitis epidemic caused by the virus of lymphocytic choriomeningitis, Ant. v. Leeuwenhoek 14: 33, 1948.
- Adams, R. D., and Kubik, C. S.: The morbid anatomy of the demyelinative diseases, Am. J. Med. 12: 510, 1952.
- Mollaret, P.: La méningite endothélioleukocytaire multirécurrente bénigne. Syndrome nouveau ou maladie nouvelle. Documents humoreaux et microbiologiques, Ann. Inst. Pasteur 154: 1, 1945.
- Nordwall, G.: Über fälle zellulärer, aseptischer Meningitis, Acta psychiat. et neurol. 9: 285, 1934.
- Sabin, A. B., Eichenwald, H., Feldman, H. A., and Jacobs, L.: Present status of clinical manifestations of toxoplasmosis in man, J. A. M. A. 150: 1063, 1952.
- Mosberg, W. H., Jr., and Arnold, J. G.: Torulosis of the central nervous system: review of the literature and report of five cases, Ann. Int. Med. 32: 1153, 1950.

- Merritt, H. H., and Moore, M.: Acute syphilitic meningitis, Medicine 14: 119, 1935.
 Farmer, T. W., and Janeway, C. A.: Infections with the virus of lymphocytic choriomeningitis. Medicine 21: 1, 1942.
- 48. Duncan, P. R., Thomas, A. E., and Tobin, J. O. H.: Lymphocytic choriomeningitis, review of 10 cases. Lancet 1: 956, 1951.
- 49. Kolmer, J. A., Freese, A. E., Matsunami, T., and Meine, B. M.: Studies of the cerebrospinal fluid in acute anterior poliomyelitis, Am. J. M. Sc. 154: 720, 1917.
- 50. Merritt, H. H., and Fremont-Smith, F.: The cerebrospinal fluid, 1937, W. B. Saunders Company, Philadelphia, p. 94.
- 51. Lillie, R. D., and Armstrong, C.: Pathologic reaction to the virus of lymphocytic choriomeningitis in guinea pigs, Pub. Health Rep. 59: 1391, 1944.
- 52. Armstrong, C., Wooley, J. G., and Onstott, R. H.: Distribution of lymphocytic choriomeningitis virus in the organs of experimentally inoculated monkeys, Pub. Health Rep. 51: 298, 1936,
- 53. Scott, T. F. McNair, and Rivers, T. M.: Meningitis in man caused by a filterable virus. I. Two cases and the method of obtaining a virus from their spinal fluids, J. Exper. Med. 63: 397, 1936.
- 54. Smadel, J. E., Green, R. H., Paultauf, R. M., and Gonzales, T. A.: Lymphocytic choriomeningitis: two human fatalities following an unusual febrile illness, Proc. Soc. Exper. Biol and Med. 49: 683, 1942.
- 55. Findlay, G. M., Alcock, N. S., and Stern, R. O.: The virus aetiology of one form of lymphocytic meningitis, Lancet 1: 650, 1936.
- 56. MacCallum, F. O., and Findlay, G. M.: Lymphocytic choriomeningitis. Isolation of the virus from the nasopharynx, Lancet 1: 1370, 1939.
- 57. Barker, L. F., and Ford, F. R.: Chronic arachnoiditis obliterating the spinal subarachnoid space, J. A. M. A. 109: 785, 1937.
- 58. Machella, T. E., Weinberger, L. M., and Lippincott, S. W.: Lymphocytic choriomeningitis. Report of a fatal case with autopsy findings, Am. J. M. Sc. 197: 617, 1939.
- 59. Wendkos, M. H., and Noll, J.: Myocarditis caused by epidemic parotitis, Am. Heart J. 27: 414, 1944,
- 60. Rosenberg, D. H.: Acute myocarditis in mumps (epidemic parotitis), Arch. Int. Med. 76: 257, 1945.
- 61. Armstrong, C.: Some recent research in the field of neurotropic viruses with especial reference to lymphocytic choriomeningitis and herpes simplex, Mil. Surgeon 91: 129,
- 62. Gordon, J. E., and Heeren, R. H.: The epidemiology of mumps, Am. J. M. Sc. 200:
- 63. Yager, R. H., and Gochenour, W. S., Jr.: Leptospirosis in North America, Am. J. Trop. Med. and Hyg. 1: 457, 1952.
- 64. Smadel, J. E.: Aseptic meningitis of known and unknown etiology, J. Clin. Investigation 21: 646, 1942.
- 65. Sigel, M. M.: From table in Chapter on Viral Encephalitides in Coriell, L. L., Principles of internal medicine, 1950, Blakiston Co., Philadelphia, p. 1065.
- 66. Broom, J. C.: Leptospirosis in England and Wales, Brit. M. J. 2: 689, 1951.
- 67. Kane, L. W., and Enders, J. F.: Immunity in mumps. III. The complement-fixation test as an aid in the diagnosis of mumps meningo-encephalitis, J. Exper. Med. 81: 137,

RELATIONSHIP OF ADIPOSITY TO SERUM CHO-LESTEROL AND LIPOPROTEIN LEVELS AND THEIR MODIFICATION BY DIETARY **MEANS***

By Weldon J. Walker, Lt. Colonel, MC, F.A.C.P., Fort Sam Houston, Texas

ATHEROSCLEROSIS is now the leading single cause of death in the United States.1 In a study of 1,250 consecutive necropsies on individuals dving after 35 years of age, Wilens 2 found the incidence of general atherosclerosis directly proportional to the amount of adipose tissue deposited throughout the body. In each decade the obese had the highest incidence of severe atherosclerosis and the poorly nourished the lowest. The patients with average nutrition had less severe atherosclerosis than the obese, but more than the poorly nourished. Numerous insurance studies 3, 4, 5 have indicated an increased mortality rate from degenerative cardiovascular disease in overweight individuals and a decrease in those who are underweight.

Several investigators have pointed out that in certain geographic locations, e.g., China,6 Okinawa7 and Costa Rica,8 the native population is singularly free of atherosclerosis and has low serum cholesterol levels. Most authors have attributed this to the low cholesterol and/or low fat content of the native diets. However, since both cholesterol and fat are readily formed in the human body, and since these populations are in general poorly nourished, it would seem equally reasonable to attribute the low incidence of

atherosclerosis to the virtual absence of obesity.

Since we will be discussing overweight and underweight, let us look first at a Metropolitan Life Insurance table purporting to show the ideal weight for height of men and women (table 1). These weights approximate the average found in adults aged 25 to 30 years. For convenience the table is arranged to show height with shoes, and weight of clothed individuals. Weights shown are for persons of medium frame. To obtain ideal weights for individuals of small frame subtract 5 per cent; for those of large frame, add 5 per cent. This, unlike most tables, allows no increase in weight with advancing years. Such tables merely reflect the increased incidence of obesity with age. As a matter of fact, muscle mass progressively diminishes after the age of 25.2 The body weight therefore should actually be less at age 50 than at 25, and this is borne out by mortality figures."

It is increasingly evident that in man there is a general correlation between the incidence of atherosclerosis and high levels of serum cholesterol.

* Presented at the Thirty-Fourth Annual Session of the American College of Physicians, Atlantic City, New Jersey, April 14, 1953.

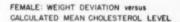
This study was conducted while the author was working in Dr. Samuel A. Levine's department at the Peter Bent Brigham Hospital, Boston, Massachusetts.

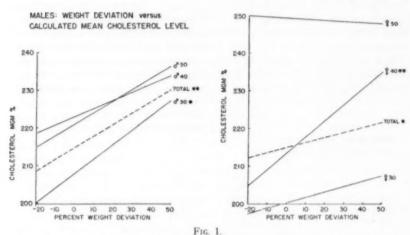
Table 1
Ideal Weights for Height for Adults of Medium Frame*

	Weight in Pounds (as ordinaril dressed)			
Height (with shoes)	Men	Women		
5 feet		116		
5 feet 1 inch		118		
5 feet 2 inches	129	121		
5 feet 3 inches	132	124		
5 feet 4 inches	135	128		
5 feet 5 inches	139	131		
5 feet 6 inches	142	135		
5 feet 7 inches	146	139		
5 feet 8 inches	150	142		
5 feet 9 inches	155	146		
5 feet 10 inches	158	150		
5 feet 11 inches	162	153		
6 feet	167	157		
6 feet 1 inch	172			
6 feet 2 inches	178			
6 feet 3 inches	183			

* After "Ideal Weights for Men," Statistical Bulletin, Metropolitan Life Insurance Company, 24: 6–8 (June) 1943; and "Ideal Weights for Women," Statistical Bulletin, Metropolitan Life Insurance Company, 23: 6–8 (Oct.) 1942.

Dr. Gofman, of the University of California, believes that the Sf 12-20 and Sf 20-100 lipoprotein fractions afford a better index of the tendency to form atherosclerosis. 10, 11 In view of the foregoing considerations, it seemed desirable to study the relationship between the degree of adiposity and levels of serum cholesterol and lipoproteins in a cross section of the American populace which presumably ingested a representative American diet. Framingham Heart Program, which has been described elsewhere.12 is studying such an adult group. Dr. Donald Love and I selected at random the records of 1,000 individuals from this group between the ages of 30 and 60 years. The age, sex, weight, height, serum cholesterol and Sf 12-20 level were extracted from each record. All cholesterol determinations were done by the laboratory of the Framingham Heart Disease Epidemiology Study and all Sf 12-20 determinations were done by the Donner Laboratory under the direction of Dr. John Gofman, Berkeley, California. Of the group, 465 were males and 535 females. Using Metropolitan Life Insurance tables as an index,13,14 the expected normal weight for height was recorded and the per cent deviation from normal calculated. Dr. Hugo Muench, Professor of Biostatistics at the Harvard School of Public Health, then analyzed the data and charted the calculated mean values by sex and Figure 1 indicates that generally the mean cholesterol level increased with increasing weight. This was more marked for males than for females, but generally was of a low degree of significance. Each group showed a definite progression with increasing weight except the women between 50 and 60 years, in whom the calculated mean value showed no change. However, this group of 134 women was hardly a representative group in that only eight were underweight, 107 were definitely overweight,

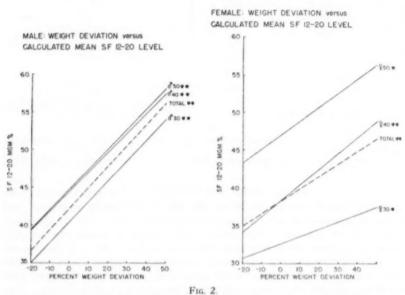




*Indicates a statistically significant trend that would occur as a chance observation less than once in 20 times.

** Indicates a statistically highly significant trend that would occur as a chance observation less than once in 100 times.

and the mean serum cholesterol level was high for the entire group. An asterisk indicates that the trend of that line is statistically significant and would have occurred as a chance observation less than once in 20 times. Two asterisks indicate a statistically highly significant trend which would occur as a chance observation less than once in 100 times. If there is no asterisk, the trend is not statistically significant. Figure 2 indicates that there was a much more marked elevation of the mean Sf 12-20 level with increasing weight which was statistically significant in each decade. steepness of the lines indicates that this was again more marked for males than for females, and coincides with insurance experience that men tolerate obesity less well than women. Women of comparable weight showed a progressive increase in Sf 12-20 levels with age, while men showed only a slight increase. Compared with males of similar age and weight, females in the fourth decade had definitely lower levels, while those in the sixth decade were higher. This agrees with the clinical observation that men get atherosclerosis earlier than women, who rarely manifest it before the menopause,15 and suggests they lose this hormonal protection at about that time. You will note that underweight individuals have lower levels than those of "normal weight." Similarly, underweight individuals show less atherosclerosis at necropsy, and insurance studies indicate that those approximately 15 per cent underweight have greatest longevity.8 These all suggest that current concepts of normal and ideal weight may need revision. However, even by current standards 624 of these 1,000 individuals were more than 5 per cent overweight. This may explain why Americans beyond age 45 do not live so long as Europeans. An article by Gofman and Jones 11 on the relationship between obesity and these levels based on a study of 241 individuals reported the same general trend but a less marked correlation with obesity for both cholesterol and the Sf 12–20 fraction. Unlike our study, in which values were correlated with per cent deviation from normal weight, their calculations were based on pounds over- or underweight. Twenty pounds over or underweight would have a very different



* Indicates a statistically significant trend that would occur as a chance observation less than once in 20 times.

** Indicates a statistically highly significant trend that would occur as a chance observation less than once in 100 times.

implication concerning relative leanness or adiposity for a person of five feet than for one six feet, two inches in height; therefore, per cent deviation from normal would seem to be a more precise manner of defining degree of obesity unless all subjects were of identical height. This could well explain why we found more significant correlations.

There is increasing evidence that atherosclerosis is not an inevitable concomitant of aging but is, rather, a pathologic process, one that sometimes is present in children, yet may be absent even in the aged. Furthermore, it appears to be a reversible process. Experimental atherosclerosis in animals is readily reversed by altering the dietary factors that produced it.¹⁷

Necropsies on semistarved individuals dying during the siege of Leningrad showed much less atherosclerosis than was previously encountered in individuals dying at a similar age. Wilens noted that, except for calcified plaques, obese individuals who died of terminal wasting diseases showed much less atherosclerosis than individuals of comparable obesity who maintained their corpulence until the time of death.

The finding of a positive relation between obesity and serum cholesterol and Sf 12–20 levels immediately posed the question of whether weight reduction would lower these levels. Several workers have reported that low cholesterol, low fat diets such as the rice diet are often associated with lowering of these values. However, such diets are bulky and unpalatable, and are usually associated with considerable weight loss. In one published study those on the low cholesterol, low fat diet had an average weight loss of 21 pounds, while the controls lost no weight. This would cause one to wonder if the results achieved were due to the weight loss or to the restriction of fat and cholesterol, which, after all, are both readily formed in the body. In conjunction with the Department of Nutrition of the Harvard School of Public Health, the influence of weight loss upon the serum cholesterol and several classes of lipoproteins was investigated in a group of 39 human subjects from the Medical Clinics of the Peter Bent Brigham Hospital.

STUDY

Of the 39 patients studied, 29 had definite cardiovascular disease, four probable cardiovascular disease and six no evident cardiovascular disease. At the beginning of the study the group had sustained 26 myocardial infarctions, one had a hemiplegia, one had lost a leg, one had thrombosis of the abdominal aorta, 15 had frequent anginal attacks, and 10 were hyper-The youngest patient was 29, the oldest 68. Ten were below 40 years of age, the remaining 29 above 40. Eleven were females, 28 males. No patient with congestive heart failure was included, since his weight would be an unsatisfactory index of altered body fat. None was receiving digitalis. None received heparin immediately before or during the study. continued to take nitroglycerin and phenobarbital. All were studied as outpatients. Each patient who adhered to the prescribed diet and sustained a weight loss in excess of 5 per cent of his normal weight is included in this report. The patients' initial weights varied from "ideal" by Metropolitan Life Insurance Tables to 50 per cent above ideal weight. However, only a few would be classed as obese at the start of the study.

DIET

Because of known cardiovascular disease most patients were on a diet low in cholesterol prior to this study. They were asked to continue their accustomed diet without weight change while control blood specimens were taken. With the onset of caloric restriction they were given a diet containing approximately 1,000 calories, with 100 gm. protein, 20 gm. fat, and 100 gm. carbohydrate; this included the mandatory daily ingestion of two eggs to insure an intake of at least 600 mg. cholesterol in addition to that usually contained in such a reducing diet. They were thus on a diet containing more than their accustomed cholesterol intake, and most lost weight rapidly enough to ensure the metabolism of considerable endogenous fat. During the weight maintenance period that followed, the caloric intake was liberalized individually by additions to the carbohydrate and protein components of the diet. Fat and cholesterol intakes were largely unchanged.

LABORATORY PROCEDURES

Except for patients who lived long distances from the clinic, two or more control determinations were taken prior to starting the dietary regimen. Control values represented the average of two or more determinations in 29 cases and of a single determination in 10 cases. Blood specimens consisted of 30 ml. blood, the serum of which was extracted and transferred to the laboratory of the Harvard School of Public Health on the day blood samples were drawn. A determination of total serum cholesterol, Sf 12–20, Sf 21–35, and Sf 35–100 lipoprotein, was made on each specimen of serum.*

Table II*

The Reproducibility of the Laboratory Methods during the Period of This Study

Standard Error of Duplicates† mg. %
10.7
4.9
3.1
7.7

^{*} From Am. J. Med.11

† Standard Error of Duplicates = $\sqrt{\frac{\epsilon \Delta^2}{2K}}$, where K = number of pairs, Δ = difference between duplicate analyses.

Blood samples were usually obtained three to four hours postprandial and were obtained at the same time of day for each patient during the period of the study. Serum specimens were usually obtained a week or more apart during the control period, at two or three week intervals during the weight losing period, and at one to two month intervals after the weight had become stabilized at its lower level. Duplicate reproducibility of laboratory methods was constantly checked during the study and is indicated in table 2.

RESULTS

It was not possible to induce all patients to reduce their weight to socalled "ideal" levels. The group accomplished and maintained a weight

^{*}These determinations were done under the supervision of George V. Mann, M.D., and Eleanor Y. Lawry, Ph.D., in the Department of Nutrition, Harvard School of Public Health.

TABLE III
Serum Lipid of 39 Subjects Who Lost 5 Per Cent or More of Their Desirable Weights*

Fraction	Control	Final	
Sf 12-20	62	48†	
Sf 21-35	34	22†	
Sf 35-100	88	431	
Cholesterol	283	263	

* Mg./100 c.c.

† Indicates that the change is statistically significant.

loss varying from seven to 40 pounds, with an average loss of 19 pounds. Final weights varied from 14 per cent below to 40 per cent above so-called ideal weight. At the time of this tabulation patients had been followed for periods of from two to 16 months, with an average of eight months, comprising in all 312 subject months of observation. In each case final values represent the average figure of the two most recent serum specimens obtained. The rate of weight loss among the 39 subjects varied considerably, with a mean value of 1.6 pounds per week during the weight-losing period. Weight loss was associated in most subjects with a reduction of all three categories of serum lipoproteins. This reduction of lipoproteins was most marked for the Sf 35–100 fraction, but was statistically significant for the Sf 12–20 and 21–35 as well. There was some reduction in cholesterol levels but this was not statistically significant. Table 3 indicates mean control and final

TABLE IV

The Response of the Serum Lipoprotein and Cholesterol Levels in 32 Individuals
Losing Weight When Grouped According to Initial Sf 12–20 Level

	Relative Weight	Rate of Wt. Loss Av. Days Losing	Sí 12-20 mg. %	Sf 21-35 mg. %	Sf 35-100 mg. %	Cholestero mg. %
**************************************	Group 1	Sf 12-20 ≥ 80) mg. % (10	0 subjects)		
Control Losing Maintenance	1.16	103.7	99.0† 69.6 65.9	56.2† 26.0 25.8	120.5† 28.7 37.0	319 291 279
	Group II	Sf 12-20 50-7	79 mg. % (12 subjects)		
Control Losing Maintenance	1.16	112.9	63.9* 51.5 53.0	34.3° 23.8 25.8	90.2* 46.5 57.3	269 262 270
	Group III	Sf 12-20 < 5	60 mg. % (10 subjects)		
Control Losing Maintenance	1.17	99.7	29.6 28.3 27.8	21.4 16.9 17.5	68.8 32.7 36.7	247 239 231

^{*} Indicates that the change is statistically significant.

Indicates that the change is statistically highly significant.

[†] Indicates that the change is statistically highly significant.

values for the various fractions for the entire 39 patients studied. Twentynine patients had a sustained lowering of Sf 12-20 levels, while 10 showed no change or a slight increase following weight reduction. However, these in general had low initial levels. This marked individual variation is indicated in the following table. At the time of this report 32 subjects had accomplished all three phases of the study, i.e., control, losing and maintenance. Table 4 shows them grouped according to their initial Sf 12-20 Those with initially high Sf 12-20 levels showed rather marked reduction in all lipoprotein levels, while those whose initial Sf 12-20 was low generally showed little reduction in any of the lipid levels. Patients with high Sf 12-20 levels tended to show higher values for all other fractions. including total cholesterol. While those who started with highest Sf 12-20 levels showed the greatest lowering with weight loss, they failed to reach a common level with the others but tended to maintain their position in rank according to the initial levels. Similarly, if grouped according to the initial cholesterol level, those with initial values above 300 showed the most marked fall of all components, those whose cholesterol started between 250 and 300

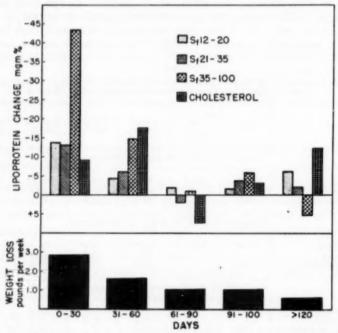


Fig. 3. The change of serum lipid levels as related to rate of weight loss. The data are mean values for 25 subjects who had initial Sf 12-20 levels above 50 mg. %. (From Am. J. Med.²¹)

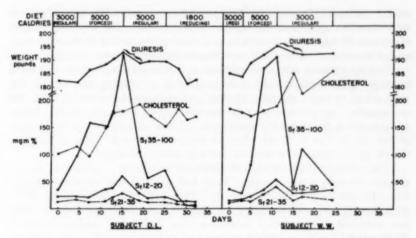


Fig. 4. The effect on serum lipids of a high caloric diet low in fat and cholesterol but liberal in protein. All charted cholesterol and lipoprotein values represent the means of duplicate determinations. (From Am. J. Med.²¹)

mg. showed a moderate reduction, and those with initial cholesterol levels below 250 generally showed little reduction in any values. The sensitivity of the serum lipids to weight loss was thus greater in individuals with high initial levels of either serum cholesterol or the Sf 12–20 class of lipoprotein.

It soon became apparent that rather marked reduction in lipoprotein levels often occurred early during the period of weight loss. Figure 3 shows this in graphic form for the 25 patients who had initial Sf 12-20 levels above 50 mg./100 c.c. This confirms an earlier report by Walker and Wier 22 that, contrary to popular medical belief, rapid weight loss is usually associated with lowering, not elevation, of serum lipid levels. In fact, this prompt reduction in lipoprotein levels suggested that negative caloric balance depressed these levels independently of weight loss per se. If such a relationship of caloric balance to serum lipid levels exists, then positive caloric balance would be expected to elevate those levels. To test this hypothesis, two normal adult volunteers (Dr. Donald Love and myself) were studied during a period of positive caloric balance with weight gain while consuming a very low fat, low cholesterol diet which was liberal in protein. After measurement on a weight maintenance control period of two weeks, rapid force feeding of this same diet was begun. Dr. Love gained 10 pounds in 11 days, and I gained 11 pounds in only nine days (figure 4). During this short period of time we both showed a threefold increase in our Sf 12-20 levels and an even greater increase in the 35-100 levels. These elevated levels fell abruptly on termination of force feeding. Serum cholesterol levels showed a more delayed rise, which continued beyond the period of positive

caloric balance. To minimize the possibility of error, all determinations were done in duplicate in this study. The diets contained less than 15 gm. of fat and 50 mg. of cholesterol per day during the period of force feeding, so this increase of serum lipids must be attributed to non-fat calories.

Twenty patients who had achieved a significant weight loss and were holding their weight at a constant level while consuming two eggs a day were asked to avoid abruptly all eggs and cholesterol-containing foods for two months in an effort to evaluate the contribution of the egg lipids. Other components of the diet were unchanged. There was no change in the lipoprotein levels, but a 20 mg. drop in serum cholesterol. The statisticians

inform me, however, that this was not a significant change.

Two subjects died during the period of this study. Each was known to have coronary artery disease. Each had accomplished significant weight loss—12 and 22 pounds, respectively. One had lowered his serum lipids with this regimen and the other had not. Of the 37 living patients, none has sustained a myocardial infarction since beginning weight reduction. Thirteen of 15 patients suffering from angina have reported significant improvement or disappearance of their angina, but, as we all know, this is a difficult symptom to appraise. The hypertensive patients showed an average drop of 21 mm. Hg in their systolic pressures and 11 mm. Hg in their diastolic. Twenty-five patients had ballistocardiograms before and after weight reduction; about half showed apparent improvement of the ballistocardiographic pattern.

DISCUSSION AND SUMMARY

This study would indicate that there is in general a direct relationship between state of nutrition and level of Sf 12-20 lipoprotein and a definite. though less marked, correlation with serum cholesterol. This relationship is more marked in men than in women. Premenopausal women seem to have lower serum cholesterol and Sf 12-20 levels than men of comparable age and state of nutrition, or than postmenopausal women. Weight reduction without dietary cholesterol restriction was associated with significant reduction of the serum Sf 12-20, Sf 21-35 and Sf 35-100 in patients whose initial levels were elevated. There was a less significant fall in total serum cholesterol levels. It might be argued that the reduced lipid levels were due to the decreased dietary fat intake inherent in a weight reduction program. However, if dietary fat elevates serum lipid levels other than through its caloric contribution, and there is some evidence that it does,23 it must exert its effect at a point other than at the metabolic level, such as enhancing the absorption and reabsorption of cholesterol in the gut, since during rapid weight reduction, when patients were metabolizing large amounts of endogenous fat, lipoprotein levels were often lowest. In some individuals lipoprotein levels are extremely sensitive and promptly respond to either positive

or negative caloric balance, irrespective of dietary fat or cholesterol. This study does not claim conclusively to exclude dietary fat or cholesterol as important causal factors in the genesis of atherosclerosis, but it does suggest that in humans total caloric intake may be a much more important factor. A similar study, in which weight reduction was achieved without reducing the dietary fat, would be of extreme interest. If, as seems likely, elevated serum lipid levels contribute to the causation of atherosclerosis, then weight reduction is a proper treatment for this disease. In our present state of knowledge, it is probably the most effective preventive and therapeutic measure available.

BIBLIOGRAPHY

- Prevention of Heart Disease: A Summary. The American Heart, April-June, 1951,
 P. 4. Published by Am. Heart Assn.
- Wilens, S. L.: Bearing of general nutritional state on atherosclerosis, Arch. Int. Med. 79: 129, 1947.
- Armstrong, D. B., Dublin, L. I., Wheatley, G. M., and Marks, H. H.: Obesity and its relation to health and disease, J. A. M. A. 147: 1007 (Nov. 10) 1951.
- Dublin, L. L., and Marks, H. H.: The influence of weight on certain causes of death, Human Biol. 2: 159 (May) 1930.
- Dublin, L. I., and Marks, H. H.: Mortality among insured overweights in recent years, read at the Sixtieth Annual Meeting of the Association of Life Insurance Medical Directors of America, October 11-12, 1951.
- Snapper, I.: Chinese lessons to Western medicine, 1941, Interscience Publishers, New York, p. 160.
- 7. Steiner, P. E.: Necropsies on Okinawans, Arch. Path. 42: 359, 1946.
- Antischkow, N.: Pathologische Anatomie und allgemeine Pathologie der Arteriosklerose, in Conference internationale de pathologie geographique, Utrecht, p. 44-97, A. Oosthoek, publisher, 1934. Quoted by Wilens, S. L.: Bearing of general nutritional state on atherosclerosis, Arch. Int. Med. 79: 129, 1947.
- Evans, F. A.: Obesity, in Diseases of metabolism, edited by G. G. Duncan, 2nd Ed., 1947,
 W. B. Saunders Co., Philadelphia, p. 522-549.
- Gofman, J. W., Jones, H. B., Lindgren, F. T., Lyon, T. P., Elliott, H. A., and Strisower, B.: Blood lipids and human atherosclerosis, Circulation 2: 161, 1950.
- Goíman, J. W., and Jones, H. B.: Obesity, fat metabolism and cardiovascular disease, Circulation 5: 514, 1952.
- Dawber, T. R., Meadors, G. F., and Moore, F. E.: Epidemiological approaches to heart disease: the Framingham study, Am. J. Pub. Health 41: 279, 1951.
- "Ideal weights for women," Statistical Bulletin, Metropolitan Life Insurance Company 23: 6 (Oct.) 1942.
- "Ideal weights for men," Statistical Bulletin, Metropolitan Life Insurance Company 24: 6 (June) 1943.
- Ackerman, R. F., Dry, T. J., and Edwards, J. E.: Relationship of various factors to the degree of coronary atherosclerosis in women, Circulation 1: 1345, 1950.
- 16. Reported in Time Magazine, Dec. 3, 1951, p. 57.
- 17. Katz, L. N.: Experimental atherosclerosis, Circulation 5: 101, 1952.
- Brozek, J., Wells, S., and Keys, A.: Medical aspects of semistarvation in Leningrad (siege 1941-1942), Am. Rev. Soviet Med. 4: 70 (Oct.) 1946.

- Starke, H.: Effect of the rice diet on the serum cholesterol fractions of 154 patients with hypertensive vascular disease, Am. J. Med. 9: 494, 1950.
- Morrison, L. M.: Reduction of mortality rate in coronary atherosclerosis by a low cholesterol—low fat diet, Am. Heart J. 42: 538, 1951.
- Walker, W. J., Lawry, E. Y., Love, D. E., Mann, G. V., Levine, S. A., and Stare, F. J.:
 The effect of weight reduction and caloric balance on serum lipoprotein and cholesterol levels, Am. J. Med. 14: 654, 1953.
- Walker, W. J., and Wier, J. A.: Plasma cholesterol levels during rapid weight reduction, Circulation 3: 864, 1951.
- Hildreth, E. A., Mellinkoff, S. M., Blair, G. W., and Hildreth, D. M.: The effect of vegetable fat ingestion on human serum cholesterol concentration, Circulation 3: 641, 1951.

MANAGEMENT OF CEREBRAL VASCULAR ACCIDENTS *

By J. M. NIELSEN, M.D., F.A.C.P., Los Angeles, California

Cerebral vascular accidents are usually thought of as thrombosis, hemorrhage and embolism. However, subarachnoid hemorrhage and subdural hematoma are also vascular accidents. Neoplasms come in for differential diagnosis in many cases.

I. CEREBRAL THROMBOSIS

Much has appeared in the literature in the last few years about the treatment of cerebral thrombosis with stellate block or intravenous injection of procaine. Let us face clearly that there is no treatment as yet which will dissolve a clot in a cerebral blood vessel. It should have been emphasized that the treatment mentioned is for *threatened* thrombosis. It must be given before a thrombosis has actually developed. It so happens that thrombosis is often heralded by recognizable signs hours or days before it develops. For this reason it is quite possible to institute treatment in time in many cases.

It has gradually come to be realized that when the stage is set by arteriosclerotic, rheumatic or syphilitic disease of the cerebral blood vessels, the factor precipitating thrombosis is a general lowering of circulatory efficiency. For this reason a coronary occlusion may cause a cerebral thrombosis, and even a bleeding peptic ulcer or an emotional shock may precipitate it.

Our present knowledge of cerebral circulation has been greatly advanced by angiography. It is known that it takes blood four and one-half seconds to pass from the internal carotid artery to the jugular vein. Before thrombosis occurs in a cerebral artery the circulation slows down considerably, and this slowing is manifested by paresthesias or mild weakness or, perhaps, by visual disturbances. In some instances as many as five or six such warnings appear before a clot forms. In one case six episodes of hemiplegia occurred in 12 hours before the actual irreversible thrombosis developed. It is during this preliminary phase of threatened thrombosis that stellate ganglion block or infusion of procaine solution is efficacious. It is the too tardy use of the remedies which has created, after a wave of optimism, a conviction of futility of the modern management.

If the patient can be reached within a few hours of the onset of what appears to be cerebral thrombosis, the physician should institute one of two methods. If he is skilled in a novocain block of the stellate ganglion, he

^{*} Presented at the Thirty-Fourth Annual Session of the American College of Physicians, Atlantic City, New Jersey, April 16, 1953.

may utilize that knowledge. The ganglion on the side opposite the hemiplegia is the one to be treated. If the injection is successful, an ipsilateral Horner syndrome with ptosis of the upper eyelid and miosis should appear in 15 minutes. If the physician is not skilled in the use of stellate block he can give, just as effectively, an intravenous infusion of 500 mg. of procaine in 500 c.c. of normal saline in two hours. This treatment is available to any practitioner. Either method relieves vasospasm and tends to speed up the circulation. As stated, if a clot has formed it does no good, but neither does it do any harm. The infusion technic is as good for cerebral embolism as for threatened thrombosis, but it is bad for cerebral hemorrhage.

Many students doubt that spasm of cerebral blood vessels occurs. Those who observe angiography do not doubt it. In fact, Villaret and Cachera observed spasm through skull windows in dogs. They found that injection of embolic material into one branch of a cerebral artery produced spasm in the entire artery. Those who do angiography commonly use an antispasmodic drug to prevent the complications of vasospasm.

Before one treats a given patient for threatened cerebral thrombosis one should be almost certain of the diagnosis. The following points are of considerable help:

1. Thrombosis occurs during rest, not during physical activity; hence it tends to develop at night.

Thrombosis does not happen suddenly, like hemorrhage or embolism.

3. In threatened thrombosis the spinal fluid may show at most a few red blood cells whereas in intracerebral hemorrhage of any size there is considerable blood in the fluid. Embolism usually causes at least some blood to appear in the fluid. We must concede, however, that at times, because of lack of history, thrombosis may seem to appear suddenly, and that a hemorrhage well walled off may show no blood in the spinal fluid. It is also true that neoplasm at times occludes a blood vessel by pressure, so that what appears clinically as a thrombosis may fundamentally be neoplasm.

II. CEREBRAL EMBOLISM

Embolism is a sudden affair. If a vessel of any material size is suddenly occluded the patient drops as if shot. Examination will usually reveal an auricular fibrillation, cardiac murmur or other source of embolism. Intravenous infusion of procaine as outlined above is good treatment for the immediate problem, but the source of the embolus overshadows the problem of the moment and must have fundamental consideration.

III. CEREBRAL HEMORRHAGE

Thousands of autopsies on brains at the Los Angeles General Hospital have shown that the old concept of a massive hemorrhage from sudden blowing out of a large vessel is not common. It is far more common, and the *rule* in traumatic intracerebral hemorrhage, that a vasomotor paralysis occurs first and the hemorrhage is by diapedesis. The gross appearance of the two types of hemorrhage is quite different. A massive rupture destroys the brain substance as a bomb would, while a hemorrhage by diapedesis leaves the structures recognizable and merely infiltrated with blood.

When an intracerebral hemorrhage occurs and remains localized, without rupture into the subarachnoid space or into a ventricle, the spinal fluid, as stated, may be clear of blood and the pressure may not be greatly increased. One has focal neurologic signs as though the lesion were a neoplasm. This type is favorable for surgical drainage. If the lesion is left it becomes a foreign body and may easily cause epilepsy.

The massive cerebral hemorrhage is so serious a condition, accompanied as it usually is by coma, that there is little to be done. The spinal fluid is grossly bloody. The patient is placed with head elevated and with an

ice cap to obtain vasoconstriction.

Repeated spinal puncture is not performed because it encourages bleeding. If the patient survives the first 24 hours the prognosis is not hopeless; if he lives 48 hours his chances are good for life but poor for function.

IV. DIAGNOSIS AND TREATMENT OF UNRUPTURED OR LEAKING CONGENITAL ANEURYSM OF CEREBRAL VESSELS

Congenital aneurysms of the circle of Willis or congenital malformations tend to give symptoms before rupture and a different syndrome after leakage or frank break. The anomalies called malformations give symptoms which depend on the anatomic location, and no one syndrome can profitably be described. On the other hand, the common saccular aneurysms of the circle of Willis tend to cause headaches diagnosed as migraine.

When one keeps in mind that migraine is a clinical syndrome due to spasm or dilatation of a cerebral blood vessel, one realizes that there can be many organic causes of migraine, and aneurysm is one. Buerger's disease, rheumatic disease and meningovascular syphilis are others. For this reason persistent, recurrent migraine syndromes which remain fairly fixed anatomically (i.e., headache always in the same area, or headache associated with extraocular palsy) would arouse suspicion of aneurysm. Angiography is then justifiable.

It is important, however, to keep in mind that, while an angiogram gives us a picture and a diagnosis which is highly probable, it has no therapeutic value. When it has been shown that aneurysm is present the neurologic surgeon has a grave decision to make: Should he attempt to trap it or amputate it, or should he do a ligation of the internal carotid artery? That decision must be left to him.

After rupture or leak of an aneurysm the patient presents a different syndrome. He is usually taken with a severe localized headache, vomits, loses consciousness, or becomes at least stuporous, and then has rigidity of the neck to flexion with preserved mobility on rotation. He likely has an extraocular palsy and hence diplopia, and presents the clinical picture of meningitis. The spinal fluid is usually under increased pressure and is always bloody. If the coma is deep there may be neither nuchal rigidity nor a Kernig's sign.

Surgeons differ as to time of doing an angiogram. Some want immediate action; others wait for the clinical picture to quiet down, and make

the study after 10 days to three weeks.

When the pictures are available the statements made above hold true: one has a picture and a probable diagnosis, but therapy is still to be worked out.

We have already been confronted with "the red herring aneurysm," i.e., an aneurysm which has nothing to do with the headache. I have seen operations done for aneurysm when the cause of the pain was glaucoma. I have also seen it done when the essential difficulty was temporal arteritis, when it was tic douloureux, or when a tumor was present.

V. SUBDURAL HEMATOMA

The classic syndrome of subdural hematoma embodied a history of trauma, immediate loss of consciousness but with apparent recovery, subsequent development of headache, progressive stupor, an ipsilaterally dilated and poorly reactive pupil, hemiplegia, and signs of increased intracranial

pressure. Each of these elements needs separate evaluation.

The trauma necessary to cause subdural hemorrhage varies tremendously. In the inebriate, a class peculiarly subject to this type of hemorrhage, a history is rarely obtainable. The patient is simply found stuporous or paralyzed after an argument often said to have been friendly. In any case, the trauma need be only slight. Scientific papers have even appeared on the subject of nontraumatic subdural hematoma. One might expect to rely on physical signs of trauma, but many cases appear a week or more after the episode, when ecchymoses have disappeared. Even when history or evidence of trauma is available, one cannot be certain that the trauma is etiologic; the patient may have had a cerebral hemorrhage and have injured his head in falling.

The next item to be analyzed is that of the state of consciousness. In the classic teaching one assumes that the blow causes initial coma, that the patient recovers from that state and loses consciousness again because of the subdural bleeding and its pressure on the brain. As explained in the paragraph above, the initial coma may be absent and the patient be brought under observation in the stage of progressive stupor. I have seen such patients sent to State hospitals as mentally ill, or arrested and jailed until coma was complete. By the time coma is present a physician can usually obtain signs leading to a diagnosis.

There is nothing characteristic about the headache of subdural hematoma

except that it is severe and steady, and is usually localized to the side affected. When one is attempting to differentiate intracerebral hemorrhage the character of the headache offers little help.

The pupils in the classic case are highly characteristic. The one on the side of the hemorrhage is initially smaller while the third nerve is irritated, later larger when the nerve is paralyzed. Between these two periods the pupils are equal. The important element of pupillary findings, therefore, is reactivity to light. Regardless of size, the affected pupil reacts poorly if at all.

The hemiplegia due to subdural hematoma differs from that due to intracerebral hemorrhage or thrombosis by being spastic initially and remaining so. Incidentally, it is often ipsilateral to the poorly reacting pupil because the brain accommodates to the subdural hemorrhage by shifting across the midline. The cerebral peduncle of the opposite side thus impinges on the edge of the tentorium cerebelli and, by pressure, affects the peduncular fibers before they cross. At any rate, the hemiplegia of intracerebral hemorrhage, thrombosis or embolism is immediately flaccid and becomes spastic after many days.

The signs of increased intracranial pressure may be characteristic but they often fail. In the first place, it takes time for choking of the optic discs to occur; secondly, the spinal fluid pressure cannot be relied upon, as it is at times diminished, often normal. These variations are due to pressure on the brain stem.

On the other hand, much can be learned from the chemical characteristics of the spinal fluid. In subdural hematoma it is often pink because of injury to the arachnoid. If it is colored the fluid should be centrifuged. Crenation of the red cells and xanthochromia indicate that at least a day has elapsed since the onset of the hemorrhage. One must remember that the fluid may be clear and normal.

A roentgenogram of the head is usually valuable because most of the patients are old enough to have calcified pineal glands, and thus displacement from the midline may be determined.

From this description it must be obvious that, dependent alone on the classic clinical syndrome, one would often overlook a subdural hematoma. Yet it is one with good prognosis if properly diagnosed and treated. In good hands, trephine holes for diagnostic purposes do no harm and will lead to a cure if diagnostically positive.

Because of the difficulties of diagnosis the present-day approach to the problem of hemiplegia with coma or with unreliable or unknown history is as follows:

One makes a good general physical examination, a neurologic examination and a laboratory study. A few hours after this is completed, diabetes or hypoglycemic coma is proved or excluded, the spinal fluid characteristics are known, the pupillary reactions are determined, and it is clear whether the hemiplegia is flaccid or spastic. Now, assuming that some sort of cerebral vascular accident is the cause of the coma and that the condition of the cardiovascular system is compatible with hemorrhage, thrombosis or embolism, one must still consider subdural hematoma. If the spinal fluid is slightly pink the question of xanthochromia is important for, if the centrifuged supernatant fluid is clear, one has an acute condition, while if it is xanthochromic there was trouble before the loss of consciousness. A pink color without crenated red cells in the spinal fluid is compatible with hemorrhage, embolism or subdural hematoma, because the arachnoid may be slightly broken.

Under such circumstances one may proceed with an angiogram or with trephining to exclude or demonstrate a subdural hematoma. In good hands the burr hole procedure is less dangerous than the angiogram and will result in a cure if the hematoma is found, whereas the angiogram is more formidable and provides only a diagnosis. If the burr holes (one on each side) show no evidence of hematoma and no source of embolism can be discovered, one can proceed to treat for cerebral hemorrhage.

Accurate localization of an intracerebral hemorrhage, of a type amenable to surgical intervention, is almost impossible while the patient is in coma. Therefore, one delays until the case is studied further.

If the findings are such as to indicate cerebral thrombosis (clear spinal fluid), one can proceed with angiogram, but greater benefit is apt to accrue from intravenous procaine (500 mg. in 500 c.c. of saline) infused in two hours. While a stellate block in experienced hands is equally efficacious, the procaine method is available to any practitioner.

BIBLIOGRAPHY

- Aring, C. D., and Merritt, H. H.: Vascular disease of the nervous system, Brain 68: 28, 1945.
- 2. Bruetsch, W. L.: Rheumatic brain disease, J. A. M. A. 134: 450, 1947.
- Dublin, W. B.: Pathologic lesions of the brain associated with chronic rheumatic endocarditis and accompanied by psychosis, Dis. Nerv. System 2: 390, 1941.
- 4. Gilbert, N. C., and de Takats, G.: Apoplexy, J. A. M. A. 136: 659, 1948.
- Hamby, W. B.: Spontaneous subarachnoid hemorrhage of aneurysmal origin, J. A. M. A. 136: 522, 1948.
- 6. Leary, T.: Subdural hemorrhages, J. A. M. A. 103: 897, 1934.
- McDonald, C. A., and Korb, M.: Intracranial aneurysms, Arch. Neurol. and Psychiat. 42: 298, 1939.
- Mount, L. A.: Treatment of spontaneous subarachnoid hemorrhage, J. A. M. A. 146: 693, 1951.
- Munro, D.: Cerebral subdural hematomas; study of 310 verified cases, New England J. Med. 227: 87, 1942.
- Penfield, W.: Surgical treatment of spontaneous cerebral hemorrhage, Canad. M. A. J. 28: 369, 1937.
- Wilson, G., Rupp, C., Jr., Riggs, H. E., and Wilson, W. W.: Factors influencing the development of cerebral vascular accidents. I. Role of cardiocirculatory insufficiency, J. A. M. A. 145: 1227 (April 21) 1951.
- 12. Villaret, M., and Cachera, R.: Les embolies cérébrales, 1939, Masson et Cie. Paris.

THE TREATMENT OF HEMOCHROMATOSIS BY MASSIVE VENESECTION *

By W. D. Davis, Jr., M.D., F.A.C.P., and W. R. Arrowsmith, M.D., New Orleans, Louisiana

Hemochromatosis is a rare disease characterized clinically by the triad of cirrhosis, diabetes and bronzing of the skin. The pathologic picture is one of massive accumulation of iron pigment throughout the tissues, with particular concentration in the epithelial glands and especially the liver and pancreas.\(^1\) The lymph nodes, heart, adrenals and testes are also frequently involved. The clinical course and gross and microscopic pathologic characteristics are well known.

The etiology and pathologic physiology are far less factually established, although recent investigations have yielded fairly convincing evidence as to its pathogenesis. Contrary to earlier conclusions, there is now sound evidence that in hemochromatosis the serum iron is elevated, with a diminution and relative saturation of the total iron binding capacity of the plasma. There is also strong evidence that iron absorption is greater than normal, a fact which has been attributed to failure or improper operation of the duodenal mucosal blocking mechanism. It is also well established that human beings have no active mechanism for the excretion of iron, and that other than through bleeding only extremely small amounts (about 0.5 mg. per day) are lost by exfoliation of various cells and loss of tissue. Thus, over the years a slowly increasing load of iron saturates the iron depots and eventually most of the body tissues. Such an accumulation may occur in several different situations, a possible classification of which is:

- I. Hemochromatosis associated with anemia.
 - A. Increased iron absorption associated with anemia.
 - 1. Potentiated by transfusion.
 - Potentiated by massive oral or intravenous administration of iron.
 - B. Exogenous-pure.
 - 1. Transfusion.
 - 2. Intravenous administration of iron.

* Presented at the Thirty-Fourth Annual Session of the American College of Physicians,

Atlantic City, New Jersey, April 16, 1953.

From the Departments of Internal Medicine, Ochsner Clinic and Tulane University of Louisiana School of Medicine, New Orleans.

- Hemochromatosis with normal hematopoiesis (failure of iron rejection).
 - A. Idiopathic or congenital (American).
 - 1. Familial?
 - B. Cytosiderosis of Gillman.
 - C. Experimental hemochromatosis.
- III. Other?

In exogenous hemochromatosis failure of the mucosal block is replaced by a breakdown of transfused erythrocytes and perhaps augmented by a compensation mechanism resulting from the type or degree of anemia present. These mechanisms may be all important, as in Cooley's anemia, in which extensive deposition of pigment may occur in the absence of transfusion.10 More recently, extensive intravenous administration of iron has provided another possible means of production of exogenous hemochromatosis, as has massive oral iron therapy in susceptible patients.11 In the exogenous form the initial pattern of distribution of the stored iron differs from that of the other varieties in that in true hemochromatosis the liver and pancreas are the sites of primary deposition, whereas in exogenous hemochromatosis the elements of the reticuloendothelial system are first filled. 12, 18 As these conditions progress, however, this difference tends to be obliterated. and it is questionable whether this represents a fundamental pathogenetic difference. 12, 14 In the special type of hemochromatosis, cytosiderosis of Gillman, 15, 16 the protective mechanism seems upset by the ingestion of a grossly deficient diet, of which at least one important missing element is phosphorus, while an unusually large quantity (150 mg./day) of iron is ingested. This combination represents an ideal situation for the simultaneous development of hemosiderosis and nutritional cirrhosis, or African hemochromatosis.

Which individual mechanism or combination of mechanisms is operative in the usual case of hemochromatosis seen in this country is questionable. Althausen and co-workers ¹⁸ and Marble and Bailey ¹⁹ were unable to incriminate any of these mechanisms in a significant proportion of their series of cases. A further promising avenue of investigation, however, may be open after completion of additional studies of the increased iron absorption resulting from dietary supplements of methionine, cystine and glutamic acid.⁸ Most of these patients, however, seem to have normal hematopoietic systems, in contrast to the exogenous group with refractory anemia. In view of the apparent lack of an excretory mechanism for iron in the normal human being, phlebotomy has seemed a rational method of approach in an attempt to mobilize the tremendous burden of tissue iron in hemochromatosis.

Though unsuccessfully tried in one patient in 1942,²⁰ and suggested in the literature in 1948,²¹ massive phlebotomy was begun independently in New Orleans ^{22, 23} and Boston ¹² six and five years ago, respectively, and

has produced interesting and encouraging results. After some modifications of the initial procedures, the following therapeutic program has been adopted by us.

Initial bleedings in 500 ml. quantities daily are done to reduce the hemoglobin level to 10.5 to 11.5 gm./100 ml. and the hematocrit to about 35 per cent. Cells and plasma are separated and the plasma is replaced after each second bleeding. Thereafter, venesection is done at intervals of four to eight days, depending on the frequency needed to keep the hemoglobin at 10.5 to 11.5 gm./100 ml. Plasma is re-infused at the time of the next phlebotomy. The patient is given the usual nutritious diet for hepatic disease, containing 500 gm, of carbohydrates, 200 gm, of proteins, and as much fat as is required to make it palatable, usually about 150 gm., with supplements of Brewer's yeast powder, one-half ounce three times daily, and one shotgun therapeutic vitamin capsule daily. Insulin is used as indicated in those with diabetes, and an aluminum hydroxide gel is given to prevent decline in the pH of the gastrointestinal tract, in order to assure that most of the iron in the intestine is in the ferric instead of the ferrous state. Adequate amounts of phosphorus are automatically included in the high protein content of the diet.

In all patients treated the diagnosis was established by liver biopsy, and whenever possible serial biopsy studies were done.^{24, 25} It must be admitted, however, that in hemochromatosis needle biopsy is somewhat more difficult and rather frequently more painful than usual because of the extremely hard and resistive quality of the hepatic tissue.

Results so far have been encouraging. Of 10 patients with hemochromatosis seen since 1945, six have been adjudged suitable for trial bleeding (table 1). Of this group, one died of primary carcinoma of the liver shortly after treatment was started, and one, treated gingerly because of concomitant weakness and congestive heart failure, has had treatment too recently for evaluation. Four have had initial favorable responses. One of these, however, has been uncoöperative because he has true chronic alcoholism, and he honestly believes that there is no reason to worry about removing blood every week to cure hemochromatosis when the alcoholism is as yet an insoluble problem. Of the four patients deemed unsuitable for venesection, one had primary carcinoma of the liver, one carcinoma of the prostate, and two severe anemia. It is now believed that one of the latter (with true pernicious anemia, who responded to liver injections) should be treated, but efforts to locate him have been unsuccessful. The other was tentatively tested but did not demonstrate adequate hemoglobin regeneration.

Of initial interest and the cause of early enthusiasm was the remarkable tolerance of these patients for bleeding (table 2). In our experience, as a rule there was complete rebuilding of 2,000 to 2,500 ml. of blood in three weeks for periods of one to two years, or until iron stores had begun to be depleted. Our most enthusiastic patient had himself bled of 18 L. of blood

in 17 weeks with only a slight decrease in hemoglobin and no change in red cell count and hematocrit! Howard and Watson's patient ²⁶ had venesections of 96,400 c.c. in a little less than four years and tolerated removal of 1,200 to 1,300 c.c. at a time without difficulty. Despite the massive drain

TABLE I

Résumé of 10 Patients with Hemochromatosis Proved by Biopsy Seen since 1945. All were bled except two with anemia and two with incurable carcinoma.

Patient	Age	Sex	Date Started	Biopsy	Serial Biopsy	Results
P. S.	69	F.	3/23/47	Yes	Yes Decreased iron in sections	Spectacular subjective improvement. Complexion lighter. Liver size about same. BSP, prothrombin, B. W., fasting blood sugar all improved. Discontinued 2/13/49 Local doctor 2/30/52. Feels well except for some indigestion.
A. W.	45	M.	11/21/48	Yes	Yes Decreased iron in sections	Pronounced subjective improvement: able to care for plantation, complexion lighter, liver smaller and softer. BSP, prothrombin, fasting blood sugar all improved. BSP later showed regression and improvement related to alcohol intake. Insulin requirement less. Well in August, 1952.
G. P.	47	M.	11/26/49	Yes	Yes Disappear- ance of iron from sections	Apparently well. Works full day with no fatigue, whereas previously incapacitated. Liver tests and fasting blood sugar normal. Liver normal size and consistency; complexion normal. Last heard from March, 1953.
R. B.	49	М.	6/24/51	Yes	Refused	Initial improvement in well being and diabetes. Reluctant to con- tinue because of alcoholism. Rebellious in 1953.*
P. L.	55	М.	6/30/51	Yes (Mayo Clinic)	Yes Cancerous	Initial improvement. Wt. gain 11 lb. Complexion lighter. Ascites. Jan., 1952, downward, died 5/26/52, primary carcinoma liver.
C. S.	67	F.	11/9/52	Yes	No	Severe psychic overlay. Followed insufficiently for opinion as yet.
F. S. M.	52	M.	Not done	Yes	No	Primary carcinoma of liver.
P. N.	38	M.	Not done	Yes	No	Macrocytic anemia which re- sponded to liver injections. Lost.
W. F.	62	М.	Not done	Yes (Surgical)	No	Carcinoma prostate.
L. H.	56	M.	4/12/52 Discontinued	Yes	No	Macrocytic anemia. Little hem- atopoietic response to bleeding.

^{*} Has since started treatment again.

TABLE 11

Quantity of Blood Removed and Length of Follow-Up of Five Patients with Hemochromatosis Treated by Massive Bleeding

Patient	Bleeding (L.)	Time (Mo.)	Iron (Gm.)	Follow-up (Years
P. S.	40	22	20	6
*A. W.	40	16	20	5
G. P.	51	21	26	4
*R. B.	8	4	7	1
†B. M. U.	103	54	52	5

^{*} Includes phlebotomies done only in New Orleans. Additional ones were done at home. † Case of Howard and Watson, ** who kindly furnished data.

on protein stores that this represents, no trouble from hypoproteinemia was encountered. On the contrary, in each case except one, increase in serum albumin and total protein levels occurred. The exception was the first patient treated, a diminutive elderly lady who simply would not eat her full diet (figure 1).

Subjective improvement was noted within a few weeks after treatment was begun. Patients said they felt better for the first few days after being bled than after the blood picture had rebounded. Further subjective improvement, manifested by a feeling of greater strength, ability to work and greater endurance, was routinely reported. As an example, one * of the patients, 5 an osteopath who was formerly unable to work at all, now works 12 to 14 hours a day and delivers about 60 babies a month. Another pa-

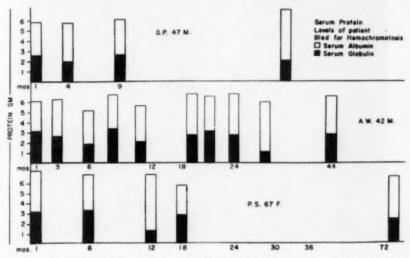


Fig. 1. Serum protein levels in patients bled for hemochromatosis. Note the higher levels of total protein and albumin toward end of bleeding.

^{*} Case previously reported in detail.



Fig. 2. Photomicrograph of serial liver biopsies from case A. W. (\times 80—H. & E. stain). A. Before phlebotomy, showing severe hemosiderosis, mild fatty infiltration, moderate inflammation and necrosis.



Fig. 2. B. After removal of about 25 gm. of iron from the system by phlebotomy, showing slight residual hemosiderosis, no fat, no inflammation, no necrosis. There is also evidence of acute regeneration.

tient,* owner of a cotton plantation, begins his day regularly at five o'clock in the morning, covers the entire plantation on horseback, and is chagrined because he gets tired by five o'clock in the afternoon.

Objective evidence of improvement has also been exhibited. In the two patients who were bled sufficiently to mobilize most of the tissue iron, a remarkable decrease in the size and consistency of the liver was noted. Serial liver biopsies in three instances demonstrated pronounced diminution and, in one case, complete disappearance of hemosiderin from the liver (figure 2). In all patients, including the one who died of carcinoma of the liver, the complexion became lighter. Those patients with abnormal liver

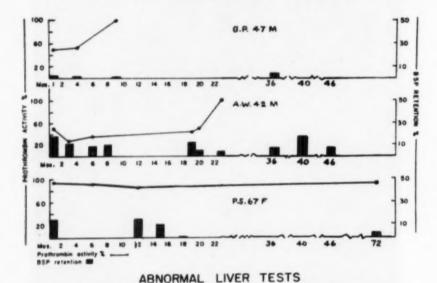
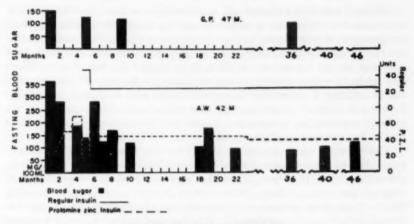


Fig. 3. Abnormal liver function tests in patients bled for hemochromatosis. The improvement is quite steady except in case A. W., who continued heavy drinking in occasional spells. These were associated with the rise in bromsulfalein retention.

function (figure 3) and those with diabetes exhibited improvement in the status of both (figure 4). The single patient with an abnormal electrocardiogram showed improvement in this abnormality after the first year, but he has since had progressive changes considered to be due to ordinary coronary arteriosclerosis rather than hemochromatosis, although this is not definitely known.

Our experience has been corroborated elsewhere, according to information kindly furnished by others interested in this problem (table 3). Finch and Finch 28 closely observed for three to five years five patients who had had

^{*} Case previously reported in detail.



STATUS OF DIABETES

Fig. 4. Status of diabetes in the two diabetic patients. There was progressive improvement in both. In case A. W. the dotted line represents dose of protamine zinc insulin and the solid line, regular insulin.

weekly phlebotomies for periods ranging from one to four years. All are doing well and none has manifested evidence of deterioration of either diabetes or liver function. They also mentioned approximately 15 other patients under treatment by various physicians in Boston for periods of from a few months to three to four years, of whom all appeared to be able to mobilize tissue iron rapidly for hematopoiesis, none has become incapacitated, and several have shown rather striking improvement in terms of liver function, sense of well being and loss of skin pigmentation.

In another patient from Boston, severe ascites and edema developed after five phlebotomies of 500 c.c. Since then he has slowly improved under a good hepatic therapeutic regimen, but the phlebotomies obviously did not help him. In reviewing his slides, however, Finch questioned whether the patient had had true hemochromatosis.

TABLE III
Results of Massive Bleeding in 30 Collected Cases of Hemochromatosis

Source	Cases	Good Results	Follow-up (Years
Finch and Finch Finch (patients treated by	6	5	3 to 5
others)	15	15 .	months to 4
Howard and Watson Anzinger	1	1	6
Gitlow and Beyers	1	1 initially	,
Authors Verified cases	15	12	1 to 6
Total (All cases)	30	27	

Howard and Watson's patient, a physician who has recorded his own experience and whose case is to be reported by them, also exhibited prompt symptomatic improvement, loss of cutaneous pigmentation and apparent decrease in the size of the liver. As in our patient, his serum albumin level increased during the period of phlebotomy despite the fact that no effort was made to return plasma to the circulation. Anzinger 20 also recently started treating a patient in Springfield, Ohio, who to date is improving. Beyers and Gitlow 30 treated at least one patient with similar results as far as blood regeneration is concerned, but further information concerning their studies has not been available to us.

Collection of these results (table 3) reveals that 12 of the 15 carefully followed patients have been able to mobilize tissue iron in response to phlebotomy, and 15 other patients have presumably also responded well, although we have not been able to secure detailed information concerning them. That those patients who are able to tolerate phlebotomy are improved initially seems established. Whether they are permanently benefited and their lives prolonged is as yet unsure, but seems likely.

COMMENT

There has been some controversy concerning the prognosis in hemochromatosis. According to Sheldon,¹ the average duration of life is 18 months after diagnosis, whereas Eusterman ³¹ estimated the average length of life after the onset of glycosuria to be about one year. Others, however, were not so pessimistic. Particularly after general use of insulin in the management of diabetes, the prognosis has seemed brighter.³²-³6 Patients still, however, eventually slipped downhill and died of hepatic coma, primary carcinoma of the liver or bleeding from ruptured esophageal varices. Introduction of the rational dietary management of hepatic disease has provided additional help but failed to halt the slowly progressive, downward course of the disease. Whether removal of the excess iron in the tissues will do more than convert their disease into simple cirrhosis or cirrhosis with diabetes, which perhaps can be definitely stabilized, must await further observation.

The question of whether the actual presence of excess quantities of iron in the tissues is damaging in itself has also been controversial. A negative opinion has been based chiefly on inability to produce experimentally cirrhosis or fibrosis of the pancreas by iron injection.³⁷ The presence of pigment in organs which seem to function normally has also been advanced as evidence in favor of this view.¹⁸ Conversely, the tissues with the highest content of iron are the ones usually involved in the production of the manifestations of hemochromatosis. Thus, in the pancreas the iron content may be 100 times normal, in the liver 50 times normal, in the heart 13 times normal.¹ In addition, the greater frequency of primary carcinoma of the liver in hemochromatosis than in cirrhosis (according to Warren and

Drake, as 18.9 per cent as opposed to 4.4 per cent) suggests an additional damaging effect of the iron pigment. Further, the rather spectacular clinical improvement of the patients in the group herein presented also suggests a definite deleterious effect of excessive iron stores in the tissues.

Therapy by repeated massive phlebotomies is limited to patients with hemochromatosis who have intact hematopoietic systems and are in sufficiently good physical condition to tolerate the bleeding. An additional disadvantage is the burdensome nature of repeated phlebotomies—so much so that it is difficult or impossible to persuade some of the patients to undertake or continue the treatment.

The applicability of the treatment to early cases of hemochromatosis, manifesting perhaps only hemosiderosis, and the relationship of these cases to minor degrees of hemosiderosis frequently seen in cirrhosis and to the elevation of serum iron seen in cirrhosis and hepatitis, must await a clear pathogenetic and pathophysiologic definition of hemochromatosis and reliable criteria for early diagnosis.

SUMMARY

Of 15 patients with hemochromatosis, including six personal and nine collected cases, 12 showed satisfactory responses to prolonged repeated bleedings. They exhibited remarkable ability to regenerate hemoglobin, mobilizing the tremendous load of excessive stored iron in doing so, and showed both subjective and objective improvement. One patient was unable to tolerate the procedure because of the development of ascites and edema, but so far no other untoward effects have been noted. The distinct impression has been obtained that these patients will have longer and more productive lives as a result of bleeding, but prolonged and carefully controlled observations will be necessary to establish this point.

BIBLIOGRAPHY

1. Sheldon, J. H.: Hemochromatosis, 1935, Oxford University Press, London.

 Marble, A., and Smith, R. M.: Studies of iron metabolism in a case of hemochromatosis, Ann. Int. Med. 12: 1592, 1939.

- Rath, C. E., and Finch, C. A.: Chemical, clinical and immunological studies on the products of human plasma fractionation. XXXVIII. Serum iron transport. Measurement of iron-binding capacity of serum in man, J. Clin. Investigation 28: 79, 1949.
- Houston, J. C., and Thompson, R. H. S.: The diagnostic value of serum iron studies in hemochromatosis; observations on seven patients, Quart. J. Med. 21: 215, 1952.
- Dubach, R., Callender, S. T., and Moore, C. V.: Studies in iron transportation and metabolism; absorption of radioactive iron in patients with fever and with anemia of varied etiology, Blood 3: 526, 1948.
- Granick, S.: Iron metabolism and hemochromatosis, Bull. New York Acad. Med. 25: 403, 1949.
- Kinney, T. D., Hegsted, D. M., and Finch, C. A.: The influence of diet on iron absorption; the pathology of iron excess, J. Exper. Med. 90: 137, 1949.
- Hegsted, D. M., Finch, C. A., and Kenney, T. D.: The influence of diet on iron absorption; the interrelation of iron and phosphorus, J. Exper. Med. 90: 147, 1949.
- Adams, W. S., Leslie, A., and Levin, M. H.: The dermal loss of iron, Proc. Soc. Exper. Biol. and Med. 74: 46, 1950.

- Houston, J. C.: Hemochromatosis and refractory anaemia, Guy's Hosp. Rep. 100: 355, 1951.
- Wallerstein, R. O., and Robbins, S. L.: Hemochromatosis after prolonged oral iron therapy in a patient with chronic hemolytic anemia, Am. J. Med. 14: 256, 1953.
- Finch, C. A., Hegsted, M., Kinney, T. D., Thomas, E. D., Rath, C. E., Haskins, D., Finch, S., and Fluharty, R. G.: Iron metabolism and the pathophysiology of iron storage, Blood 5: 983, 1950.
- Wyatt, J. P., and Goldenberg, H.: Hemosiderosis in refractory anemia, Arch. Int. Med. 83: 67, 1949.
- 14. Finch, C.: Personal communication.
- Gillman, J., and Gillman, T.: Structure of the liver in pellagra, Arch. Path. 40: 239, 1945.
- Gillman, J., and Gillman, T.: The pathogenesis of cytosiderosis (hemochromatosis) as evidenced in malnourished Africans. Gastroenterology 8: 19, 1947.
- Walker, A. R. P., and Arvidsson, U. B.: Iron intake and hemochromatosis in the Bantu, Nature. London 166: 438, 1950.
- Althausen, T. L., Doig, R. K., Weiden, S., Motteram, R., Turner, C. N., and Moore, A.: Hemochromatosis; investigation of twenty-three cases, with special reference to etiology, nutrition, iron metabolism and studies of hepatic and pancreatic function, Arch. Int. Med. 88: 553, 1951.
- 19. Marble, A., and Bailey, C. C.: Hemochromatosis, Am. J. Med. 11: 590, 1951.
- Balfour, W. M., Hahn, P. F., Bale, W. F., Pommerenke, W. T., and Whipple, C. H.: Radio iron absorption in clinical conditions; normal, pregnancy, anemia and hemochromatosis. J. Exper. Med. 76: 15, 1942.
- Schwartz, S. O., and Blumenthal, S. A.: Exogenous hemochromatosis resulting from blood transfusions, Blood 3: 617, 1948.
- Davis, W. D., Jr., and Arrowsmith, W. R.: The effect of repeated phlebotomies in hemochromatosis, J. Lab. and Clin. Med. 39: 526, 1952.
- Davis, W. D., Jr., and Laurens, H., Jr.: Correlation of results of liver function tests and liver biopsy in hepatic disease, South. M. J. 43: 217, 1950.
- 24. Davis, W. D., Jr.: Needle biopsy of the liver, New Orleans M. and S. J. 100: 159, 1947.
- Topp, J. H., and Lindert, M. C. F.: The diagnosis of hemochromatosis by means of needle biopsy of the liver, Gastroenterology 10: 813, 1948.
- 26. Howard, R. B., and Watson, C. J.: Personal communication.
- 27. Urenn, B. M.: When patients are doctors, 1952, W. W. Norton & Co., New York, p. 238.
- 28. Finch, S. C., and Finch, C.: Personal communication.
- 29. Anzinger, F. W.: Personal communication.
- Beyers, M. R., and Gitlow, S. E.: Metabolism of iron in hemochromatosis, Am. J. Clin. Path. 21: 349, 1951.
- 31. Eusterman, G. B.: Hemochromatosis, M. Clin. North America 11: 1376, 1928.
- Butt, H. R., and Wilder, R. M.: Hemochromatosis; report of 30 cases in which the diagnosis was made during life, Arch. Path. 26: 262, 1938.
- Barker, L. F.: Control of diabetes in hemochromatosis; remarkable improvement in the strength and working capacity of a patient with decrease of his pigmentation under diet and insulin, M. Clin. North America 14: 177, 1930.
- Feder, I. A., Gitman, I., and Hoffman, J. B.: Hemochromatosis, Rev. Gastroenterol. 17: 1048, 1950.
- 35. Lawrence, R. D.: Hemochromatosis, Proc. Roy. Soc. Med. 43: 356, 1950.
- 36. Lawrence, R. D.: The prognosis of hemochromatosis, Lancet 2: 1171, 1936.
- Polson, C.: The failure of prolonged administration of iron to cure hemochromatosis, Brit. J. Exper. Path. 14: 73, 1933.
- Warren, S. and Drake, W. I., Jr.: Primary carcinoma of the liver in hemochromatosis, Am. J. Path. 27: 573, 1951.

INTRA-ARTICULAR HYDROCORTISONE IN THE TREATMENT OF ARTHRITIS*

By Joseph L. Hollander, M.D., F.A.C.P., Philadelphia, Pennsylvania

For many years physicians have attempted to suppress arthritic inflammation by injecting petrolatum, jodized oil, lactic acid, procaine or antibiotics directly into the affected synovial space.1 Dr. George Thorn 2 was the first to inject compound F of Kendall (now called hydrocortisone) into an arthritic knee joint. However, as luck would have it, not only did the treated joint improve but the general condition of his patient also improved This made him assume that the particular patient was exthe next day. tremely sensitive to the systemic action of the hormone, and the profound local anti-inflammatory effect of small doses of hydrocortisone was thus obscured.

Having had the audacity, as internists, to aspirate many joints over a period of some years in an effort to learn more of the physiology and dynamic pathology of joint disease,8 we naturally assayed the effects of cortisone injected directly into the diseased joints themselves. The effect of cortisone thus used, however, was disappointingly inconsistent, short lived and minimal. When hydrocortisone became available, however, and the experiments were repeated substituting this hormone, a fairly consistent and usually quite marked amelioration of joint inflammation was noted.4 The beneficial effect from a single injection of the hormone often persisted for several weeks. Of even greater significance, however, was the fact that local amelioration was possible without any appreciable systemic hormonal effects.

These encouraging early results were later confirmed by others, 8, 6, 7, 8 and soon led us to the extensive clinical assay of intra-articular hydrocortisone reported here. Not only was it essential to be certain that the intrasynovial hormone injections actually produced a fairly lasting local ameliorating effect on arthritic inflammation, but also to detect adverse effects or even dangers, and to observe the effects of repeated injections into the same joint over protracted periods of time.

Since January, 1951, we have injected hydrocortisone into the inflamed joints, bursae or tendon sheaths of 852 patients a total of 8,693 injections. Only the generous amounts of hydrocortisone supplied by the manufacturer.

^{*} Presented at the Thirty-Fourth Annual Session of the American College of Physicians, Atlantic City, New Jersey, April 17, 1953. From the Arthritis Section, Department of Medicine, Hospital of the University of

Supported by grants from the Helon Augusta Parkhill Foundation, from Merck and Co., Inc., and from the National Institute of Arthritis and Metabolic Diseases, United States Public Health Service.

a simplified technic of joint injection, an abundant supply of arthritic patients at the Hospital of the University of Pennsylvania, and a large and diligent clinic staff have made this large series possible.

TECHNIC

Ordinary aseptic precautions, without the use of drapes or rubber gloves, have been used throughout. Local anesthesia was seldom necessary once the operator became familiar with the technic for aspirating each specific joint. It was found that the aspirating needle could be quickly, easily and relatively painlessly inserted into the synovial cavity of the knee, ankle, wrist, hip or other joint that was the major site of the arthritis. The dose of 25 mg. (more or less) of hydrocortisone suspension was injected without force, after excess synovial fluid had been aspirated.

For hydrocortisone to be effective locally, it is imperative that it be injected *into* the synovial space, where it can bathe the entire inflamed surface. Many of the failures have resulted from improper places. Int of the hormone suspension—near the joint space, but not into it.

Detailed descriptions of technic for injection of the various joints have appeared elsewhere, so only a brief recapitulation is given here. The knee joint (figure 1) is easily injected from the medial side, just dorsal to the patella. The ankle (figure 2A) is most readily aspirated from an anteromedial approach. The elbow (figure 3A) is usually injected laterally, the shoulder (figure 4) anteriorly, the wrist (figure 5) and finger joints (figure 6) dorsally, and the hip (figure 7) from an anterolateral approach. Of



Fig. 1 A. Injection of hydrocortisone into left knee. Needle is inserted medially to patella, pointed slightly posteriorly to slide between patella and patellar groove of femur.



Fig. 1 B. X-ray showing needle in place in left knee for injection.

the peripheral joints the hip is the most difficult to inject, because of its depth below the body surface. Spinal joints have been almost impossible to inject because of their anatomic structure and the large mass of overlying muscles.

RESULTS

As with any treatment in clinical medicine, this local use of hydrocortisone does not produce relief of symptoms and signs in all cases. The mode of action of hydrocortisone is still unknown. Recent experiments in our laboratory 8 have shown that the injected microcrystals of hydrocortisone disappear quickly (within two hours) from the synovial fluid and are absorbed and retained by the lining cells of the synovial membrane. Details of this study will be forthcoming in a subsequent report.

In classifying results of individual injections, we have had considerable

difficulty because of wide variation in response.

The results after injection have ranged from no improvement, or even temporary increase in inflammation, all the way to complete amelioration which has persisted for over two years. These are the extremes, and over 85 per cent of the 8,693 intra-articular injections were "successful" in that they were followed by demonstrable local improvement persisting for from three days to many weeks, with gradual relapse of the local inflammation to its pretreatment state. Repeated injections into the same joint at varying intervals reproduced, or sometimes even exceeded, the degree and



Fig. 2.4. Injection of hydrocortisone into the left ankle. Needle is inserted from anteromedial surface just above level of tip of internal malleolus to depth of about 4 cm.



Fig. 2B. X-ray showing needle in place for injection into ankle.



Fig. $3\,A$. Injection of hydrocortisone into left elbow joint. Needle is inserted parallel to ulna and just lateral to olecranon.



Fig. 3 B. X-ray photograph showing needle in place for injection into left elbow.



Fig. 4. Injection of hydrocortisone into the left shoulder joint. The needle is inserted from the anterior aspect just below the tip of the coracoid process to a depth of about 4 cm.

duration of the initial alleviation. Occasional loss of beneficial effect after succeeding injections was encountered also, but in less than 5 per cent of cases.

We have therefore arbitrarily classified as *successful* those injections which produced unequivocal improvement in symptoms and signs in the injected joint which persisted a minimum of three days. If improvement continued in a given case after one or a series of injections throughout the



Fig. 5. Injection of hydrocortisone into right wrist. A one inch, 22 gauge needle is inserted from dorsal aspect, just distal to the distal end of the radius, to a depth of about 2 cm.

study period, this was designated a "successful" case. Case failures included all those in whom the benefit was inconsistent or was insufficient in degree or duration to appear of practical value in treatment.

A summary of the results of the injections is presented in table 1. It will be noted that many more knees were injected than any other joints, and that the results in the knees were better than in the other joints. The



Fig. 6. Injection of hydrocortisone into third metacarpophalangeal joint. A one inch, 24 gauge needle is used.

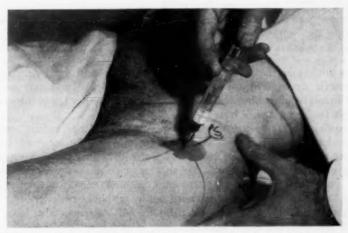


Fig. 7. Injection of hydrocortisone into left hip joint. Needle is inserted from anterior aspect at a point where vertical line from anterior superior spine of ilium and horizontal line from trochanter cross. A two inch 20 gauge needle is inserted slightly medially to a depth of about 6 to 7 cm.

knee is the largest and most accessible joint, and is most frequently disabling. Generally, the more difficult the joint to aspirate and inject, the poorer the results. This is correspondingly true with other synovial and serous cavities.

Successive re-injections have been carried out when symptoms recurred. We have re-injected a single joint as many as 47 times during the study period. Intrasynovial hydrocortisone therapy has been employed in a wide variety of rheumatic conditions, as noted in table 2. Successful results in these diverse conditions demonstrate the nonspecific nature of the alleviating action. Although most of the cases were rheumatoid arthritis or osteoarthritis, there were 63 cases of traumatic arthritis or tenosynovitis, 45 of bursitis, 21 of acute gouty arthritis, six of lupus erythematosus in which there was involvement of joints or serous membranes, three of periarteritis

TABLE I
Analysis of Results from Intrasynovial Hydrocortisone

Site of Injection	Number Given	Number Failures	Per Cent Failure
Knee	5931	341	6%
Ankle	488	74	15%
Wrist	397	131	33%
Hip	371	192	52%
Phalangeal	322	36	11%
Elbow	316	32	10%
Shoulder	308	107	34%
Other Joints	79	36	45%
Subdeltoid bursa (acute)	82	17	21%
Subdeltoid bursa (chronic)	221	113	51%
Bursae (except shoulder)	6.3	13	22%
Tendon sheaths	105	8	7%
Pleural cavity	8	4	50%
Pericardial cavity	2	2	100%
		- Common	(SECONDARIO)
Totals	8693	1106	13%

nodosa with joint inflammation, five of shoulder-hand syndrome (reflex sympathetic dystrophy), of which four were failures, and one each of hemarthrosis from parahemophilia (AC globulin deficiency), and tuberculous arthritis (to be mentioned later).

Surprisingly, the reaction of patients to this rather robust form of therapy has been excellent. Nearly all patients eagerly returned for reinjection when the beneficial effect had worn off. In many instances, we simply gave instructions to call for another appointment when necessary. Some patients have gone many months without need for further local therapy, and follow-up has been carried out by telephone or letter.

Summary of the follow-up on the first 547 patients, who have been treated and observed for at least one year, is as follows:

One hundred six (20 per cent) of these patients have obtained lasting relief of symptoms and signs of the local inflammation for at least a year

since last injected. Naturally, this includes a large number of cases of gout, traumatic arthritis, bursitis and tenosynovitis, the exacerbations of which are more or less self-limited anyhow. Also included, however, are 31 cases of osteoarthritis of the knees in which relief has persisted for more than a year following a few successive injections. There were also 14 cases of rheumatoid arthritis in which inflammation in the treated joint has not yet returned, even though continued activity may be evident elsewhere.

In 296 patients (54 per cent) the relief has been temporary, but repeated injections have successfully maintained relief for more than a year. These patients continue to receive injections at varying intervals, as needed. They are nearly all patients with rheumatoid arthritis or osteoarthritis.

TABLE II

Analysis of Results from Intrasynovial Hydrocortisone

Diagnosis	Number of Patients	Local Result			
		Case	Success	Case	Failure
Rheumatoid arthritis	376	334	(89%)	42	(11%)
Osteoarthritis (except hip)	289	245	(85%)	44	(15%)
Osteoarthritis of hip	42	20 58 25 19	(47%)	22	(53%)
Traumatic conditions	63	58	(92%)	. 5	(8%
Bursitis without arthritis	45	25	(58%)	20	(42%
Gouty arthritis (acute)	21	19	(90%)	2	(10%
Miscellaneous	16	9	(56%)	7	(44%
Totals	852	710	(83%)	142	(17%

Sixty-five patients (12 per cent) had obtained relief from their injections when last seen but have been lost to the long-term study. Fifty-eight have moved or have not reported, so that we cannot be sure whether these patients were successfully treated or have gone elsewhere seeking other therapy. Seven patients died. These were all seriously ill of diffuse collagen disease, and in none could the local use of hydrocortisone be indicted as the cause of death, either by the time interval between the last injection and death, or by the nature of the autopsy findings.

Eighty patients (14 per cent) obtained little or no relief from intraarticular hydrocortisone. Even though some of these patients obtained relief from a few of their injections, the relief was inconsistent or brief, so they were counted as complete therapeutic failures. In some, particularly those with osteoarthritis of the hip, the failure could be attributed to the technical difficulty of the injections, but in others the joint was easily aspirated and the reason for therapeutic failure remains obscure.

ADVERSE REACTIONS TO INTRA-ARTICULAR HYDROCORTISONE

In trying to observe the ancient motto of the physician, "Primum non nocare" (first do no harm), we have been gratified by the rarity and the

almost universally mild character of adverse effects from intra-articular hydrocortisone injection. Of the total 8,693 injections given, 199 (2.3 per cent) were followed by some untoward reaction. The great majority of these (156) consisted of a temporary exacerbation of the joint inflammation, which persisted from a few hours to several days, often with subsequent improvement over the pretreatment state. No definite cause for such occurrences has as yet been found, and seldom has this developed more than once in a given patient. Such exacerbations do not contraindicate further injections.

In 17 instances a hydrocortisone injection has been followed by a local weakness and feeling of instability of the treated extremity persisting for one to three days. Fifteen patients experienced a generalized weakness, vertigo and malaise after injection, which in one instance persisted about four days. The cause for these rare complications is also undetermined.

TABLE III

Incidence of Adverse Reactions in 8,696 Hydrocortisone Injections

Type	Number	Incidence
Local exacerbation (lasting 2-72 hours)	156	1.9%
Local weakness (lasting 4-96 hours)	17	0.2%
General weakness, malaise, vertigo (lasting 12-96 hours)	15	0.1701
	15	0.17%
Local urticaria at site of injection Spread of monarticular rheumatoid	4	
arthritis to other joints	2	0.02%
Infection of knee from injection	2	0.02%
Thrombophlebitis in injected leg	2	0.02%
Aggravation of tuberculous arthritis	1	$0.02\% \\ 0.02\% \\ 0.01\%$
Totals	199	2.3%

In four instances there were hives about the site of injection for some hours following. In three of these the reaction appeared to be allergy to the procaine used for local anesthesia, but in the fourth there was a cutaneous reaction to the suspending agents in the aqueous vehicle of the hormone suspension.

In two instances in which a monarticular rheumatoid arthritis was treated locally by this method the local process was suppressed but there was a concomitant spread of the arthritis to other joints. Although this has been rare, it serves to show that this method is not a complete treatment for such a systemic process, and could even be accused of converting a localized reaction to a more widespread disease.

In only two instances was a joint infection produced by intra-articular injection, and in both instances the infection responded promptly to penicillin, without apparent permanent damage to the joint. Concomitant with one of these (and in another instance without infection), a low-grade throm-bophlebitis appeared in the treated extremity after local use of hydrocorti-

sone. These responded without further complication to immobilization

and anticoagulant therapy.

A patient with tuberculous arthritis of an ankle was inadvertently included in the series through an error in diagnosis. Although the joint swelling and tenderness lessened after injection, severe relapse followed and synovial biopsy revealed the true diagnosis. Orthopedic treatment was then successfully instituted.

DISCUSSION

It cannot be overemphasized that this form of therapy is strictly for local palliation and is not a substitute for systemic therapy for any generalized rheumatic process. Likewise, supportive therapy should not be neglected when this adjunct is employed. Intra-articular hydrocortisone has proved a useful adjunct to general measures in the management of rheumatoid arthritis, osteoarthritis and gout, particularly when one or only a few joints are actively involved. For localized conditions such as bursitis, traumatic arthritis, tennis elbow and tenosynovitis such as "trigger finger," hydrocortisone injections have been successfully employed alone.

Since local hydrocortisone injections into one or two joints at a time practically obviates the danger of systemic hormonal effects, it can be used in patients in whom contraindications to systemic cortisone therapy exist. This local method has also proved valuable as an adjunct in orthopedic

surgery and in rehabilitation.

The only contraindications to the employment of intra-articular hydrocortisone are the presence of infection in or near the joint, or disease so widespread that local therapy is impractical. Arthritis of spinal joints is not amenable to this form of therapy for anatomic reasons.

There has been a tendency for internists to avoid therapy by intraarticular injection, thinking this falls more into the province of the surgeon. Since this procedure appears potentially much less hazardous than thoracentesis, abdominal paracentesis, pericardial paracentesis or lumbar puncture, we do not subscribe to such a view, and regard intra-articular injection as a procedure no more formidable than intravenous infusion, or even venipuncture. As with the latter procedures, however, skill must be developed by training and practice. Detailed instructions in technic are now available to the physician.¹

To illustrate our own confidence in the safety and efficacy of this form of therapy, the author and two associates have received injections of the hormone into a joint or bursa for localized rheumatic conditions during the past year. Our own symptomatic relief has added to our conviction that this is a useful adjunct in local treatment of rheumatic conditions. As a common saying has it, "When a bootlegger drinks his own whiskey, it has

to be good."

SUMMARY

A total of 8,693 intrasynovial injections of hydrocortisone have now been given in 852 patients with a variety of rheumatic diseases. At least partial amelioration of local symptoms and signs, often persisting for weeks or months, has resulted in most instances. Adverse effects have been rare and nearly always mild and self-limited. Although the period of observation has extended over more than two years, the treatment must still stand the further test of time before *complete* acceptance as a therapeutic agent in the local management of rheumatic diseases.

BIBLIOGRAPHY

- Hollander, J. L.: Comroe's Arthritis and allied conditions, 5th Ed., 1953, Lea and Febiger, Philadelphia, pp. 319-336.
- 2. Thorn, G. W.: Personal communication.
- Horvath, S. M., and Hollander, J. L.: Intra-articular temperature as a measure of joint reaction, J. Clin. Investigation 28: 543, 1949.
- Hollander, J. L., Brown, E. M., Jr., Jessar, R. A., and Brown, C. Y.: Hydrocortisone and cortisone injected into arthritic joints, J. A. M. A. 147: 1629, 1951.
- Stevenson, C. R., Zuckner, J., and Freyberg, R. H.: Intra-articular hydrocortisone (compound F) acetate, Ann. Rheumat. Dis. 11: 112, 1952.
- Duff, I. F., Ropes, M. W., Jessar, R. A., Steinberg, C. L., Davison, R., and Rawls, W. B.: Discussion at meeting of American Rheumatism Association, Ann. Rheumat. Dis. 11: 302, 1952.
- Kashtan, H. A.: Hydrocortisone (compound F) in arthritic joints, Harper Hosp. Bull. 10: 143, 1952.
- De Seze, S., Robin, J., Chevallier, J., and Francon, J.: Initial results with intra-articular hydrocortisone in rheumatology, Presse méd. 60: 1465, 1952.
- Zacco, M., Dohan, F. C., and Hollander, J. L.: Disposition of intra-articular hydrocortisone in articular tissues. In preparation.

GASTRODUODENAL HEMORRHAGE: DIFFICULTIES IN RECOGNITION OF LESIONS AT OPERATION BY PALPATION AND INSPECTION*

By EMANUEL M. RAPPAPORT, M.D., F.A.C.P., Jamaica, N. Y.

THERE are few problems confronting the internist more vexing yet intriguing than that of recurrent bleeding from the upper gastrointestinal tract where repeated diagnostic studies fail to disclose the source of hemorrhage. In some cases a definitive lesion is not found despite repeated exploratory operations, and occasionally the mystery remains unsolved even at post mortem.

Most frustrating and bewildering to the clinician, however, are the cases in which lesions presumed to be the cause of hemorrhage are detected by roentgenogram or gastroscopy, yet at operation the surgeon reports that "after palpation and a detailed inspection of the stomach and small intestine no pathology or cause for hemorrhage was found." To judge from the dearth of reports in the literature to the contrary, the surgeon's verdict must be considered final as to the presence or absence of gross gastric or duodenal lesions regardless of the roentgenogram or gastroscopic findings. Palpation and inspection of the stomach in the open abdomen provide a far more accurate appraisal of gross pathology than does the roentgenogram, since perigastric adhesions, large but otherwise normal mucosal folds, congenital anomalies or pressure from adjacent organs can produce roentgenologic defects which mimic many hemorrhage-producing lesions. Thus to dispute the operative findings of an experienced surgeon is usually hazardous.

It is the purpose of this communication to show that palpation and inspection of the stomach or duodenum at laparotomy are not infallible, and that occasionally major pathologic lesions may be overlooked even when the mucosal surface is examined.

The patients in this series shared several features in common. All had had recurrent episodes of bleeding from the upper gastrointestinal tract, the site of which was localized by roentgen-ray or gastroscopy, yet at operation the clinical diagnosis was discounted on the basis of negative surgical findings at the site indicated. Nevertheless, the original diagnosis was substantiated in each instance at a subsequent operation.

CASE REPORTS

Case 1. A 54 year old male executive was hospitalized December 1, 1949, because of massive melena of three days' duration. For several years he had noted occasional precordial and epigastric fullness, relieved by belching. He required transfusions totaling 4,500 c.c. before the bleeding stopped. A gastrointestinal series

^{*} Received for publication March 3, 1953.



Fig. 1a. Case 1. Large hiatus hernia demonstrated following massive hemorrhage (December, 1949). b. Filling defect of the cardia noted after hemorrhage (April, 1951). The hernia is not seen. c. Postoperative x-ray (May, 1951), showing a persistent smooth defect of the cardio-esophageal junction. At a second operation a lipofibroma was found.

on December 16 showed a reducible hiatus hernia (figure 1a). He was discharged feeling well, and he was not seen again until March 22, 1951, when he presented himself because of anorexia, loss of weight and weakness. Physical examination was essentially negative except for pallor. There was a marked anemia, with hemoglobin 52 per cent and red blood cells 2,800,000. Stools contained 4 plus occult blood. Roentgenograms showed a large filling defect of the lower end of the esophagus and the cardia (figure 1b). There was a coarseness of the mucosa of the duodenal bulb but no niche was seen. The patient was hospitalized and transfused. Gastroscopy was performed and, though no tumor was seen, it was believed that the latter was too close to the cardia for successful visualization. Since operation of a most difficult order appeared indicated, the patient was transferred to a large medical center with the diagnosis "carcinoma of the cardia and hiatus hernia," and with the recommendation that esophagoscopy be done for purposes of taking a biopsy.

The esophagoscopist reported that no neoplasm was seen in the esophagus or cardia, and hence no biopsy was taken. At operation the surgeon found a large hiatus hernia, which he repaired. No tumor was palpable in the cardia or in the lower esophagus. The duodenal bulb appeared normal. He was discharged with

the diagnosis "hemorrhage from hiatus hernia."

The patient felt well following operation and regained his lost weight. He returned for roentgenograms one month later and at this examination the same filling defect previously noted in the lower esophagus and cardia was evident (figure 1c). Its lower margin was smooth and its appearance suggested a benign tumor of the cardia. It was difficult to reconcile the roentgenogram with the operative finding, yet the patient was asymptomatic, with a normal blood count and stool negative for occult blood. In December, 1951, the roentgenologic appearance was

unchanged and the patient was still symptom-free.

On April 8, 1952, he returned for study because of recurrence of anorexia, loss of weight and melena. Again the stool contained 4 plus occult blood, and a marked anemia was present with hemoglobin 48 per cent and red blood cells 3,100,000. A final gastrointestinal series revealed the same constant defect of the cardia, and the patient was hospitalized with a diagnosis of "benign tumor of the cardia." Esophagoscopy again failed to disclose a tumor, but the instrument could not be passed into the cardia. At operation numerous adhesions were present in the upper abdomen. A definite tumor could not be palpated, so the surgeon was requested to incise the cardia, and only then could a large hemorrhagic tumor be seen occupying the cardioesophageal junction. The tumor was excised and proved to be a lipofibroma (9 by 5 by 3.5 cm.), a portion of which was covered by esophageal mucosa. The patient made an uneventful recovery and has remained well since. In retrospect it would appear that the tumor was the cause of his initial hemorrhage in 1949, but it was obscured on the roentgenograms by the large hiatus hernia.

Case 2. A 46 year old printer had a cholecystectomy for gall-stones in 1946. In July, 1951, he began to experience postprandial epigastric fullness and burning. Following roentgenograms he was told he had a duodenal ulcer, but he obtained little benefit from an ulcer régime. In November he was hospitalized because of melena, and required 1,000 c.c. transfusions. A gastrointestinal series was reported as showing a questionable deformity of the prepyloric region and a poorly filling duodenal bulb. Gastric analysis was normal. He was discharged on November 22 but re-admitted three days later because of recurrence of painless melena. Following transfusions, roentgenograms were repeated and again revealed a prepyloric deformity, but at this study the mucosa of the cardia appeared coarse and irregular (figure 2a). Because of the inconclusive diagnosis the patient was referred to the author for gastroscopy. At the latter examination, although the antral mucosa appeared hypertrophic, no significant abnormality was noted in the distal stomach. The

rugae of the anterior wall below the cardia and extending up to it were stiff and infiltrated, but no ulceration or bleeding lesion was noted. The gastroscopic diagnosis was carcinoma of the cardia, although lymphosarcoma could not be ruled out.

As in case 1, since a total gastrectomy appeared indicated, the patient was referred to a large medical center for operation. At the latter institution esophagoscopy was done but no neoplastic tissue was seen. A Papanicolaou stain of gastric contents was negative for cancer cells. At operation the surgeon reported that numerous adhesions were present between the duodenum and liver. The cardia felt normal on palpation. A soft mass was palpable in the prepyloric region, and it could be prolapsed into the duodenum. The antrum was opened and the mass proved to be redundant gastric mucosa. Nothing suggestive of carcinoma was seen and the duodenal bulb appeared normal. The redundant antral mucosa was excised and a pyloroplasty performed. The pathologic diagnosis was "hypertrophic antral gastritis."

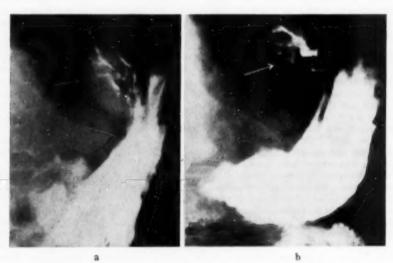


Fig. 2a. Case 2. Bizarre mucosal pattern of the cardia indicated by the arrows, interpreted by gastroscopy as carcinoma (December, 1951). b. Progression of the mucosal deformity of the cardia (August, 1952). Extensive adenocarcinoma was found at a second operation.

Postoperatively the patient showed little improvement, having the same complaint of epigastric fullness after eating. There was a slow but progressive loss of weight. In May, 1952, he began to experience constant pain in the left upper abdomen. Although he was maintained continuously on liver injections and oral hematinics, there was a progressive anemia. In August he had another episode of melena. Roentgenograms revealed a progression of the mucosal changes previously noted in the cardia (figure 2b). Gastroscopy was repeated and a polypoid carcinoma with a hemorrhagic surface was seen just below the cardia. A second operation was done and an extensive adenocarcinoma of the cardia was found. A total gastrectomy was performed, but the patient died three months later from homologous serum jaundice.

Case 3. A 54 year old female diabetic had noted vague epigastric fullness and burning of the tongue for four months. In January, 1946, roentgenograms gave negative findings, but she was told she had a low acid secretion and was placed on dilute HCl, with little relief. One month later she was hospitalized because of melena and weakness. Following transfusions, roentgenograms were reported as showing a coarse rugal pattern of the stomach, a normal duodenum and numerous diverticula of the colon. She was discharged with the diagnoses "gastritis" and "diverticulitis."

In May, melena recurred and she was again hospitalized. Roentgenograms revealed a persistent small oval defect in the upper portion of the body of the stomach near the greater curvature, suggesting a polypoid tumor (figure 3a). At operation the surgeon reported that the stomach presented no abnormality on palpation and inspection. No tumor was felt and the stomach was not opened. The duodenum

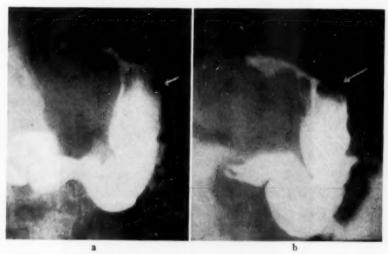


Fig. 3a. Case 3. Oval filling defect, interpreted as a polypoid tumor, indicated by the arrow (May, 1946). b. A larger defect in the same area (August, 1946), proved to be lymphosarcoma at a second operation.

and the entire small intestine were inspected and found to be normal. Many diverticula were seen in the colon. The abdomen was closed and the patient was discharged with no explanation for her recurrent bleeding.

Following operation she continued to complain of epigastric pain, anorexia and weight loss. In August she was referred here for further study. Physical examination was essentially negative except for slight tenderness in the epigastrium. Roent-genograms again showed a mucosal defect below the fundus (figure 3b). Gastric analysis with histamine revealed a maximum free HCl of 12 units. Hemoglobin was 60 per cent; red blood cells were 3,400,000; stool contained 4 plus occult blood. At gastroscopy the rugae of the upper third of the stomach were intensely hyperemic, and a trickle of blood was noted emanating from the fundus but its source could not be seen. A sessile polyp was noted on the posterior wall near the greater curvature, suggesting a small carcinoma. The lower half of the stomach showed no significant disease. At operation many adhesions were encountered in the upper abdomen

but nothing abnormal could be palpated in the stomach. When the latter was opened the rugae appeared hypertrophic but no bleeding lesion was seen. Near the greater curvature below the fundus a soft nodule, 2.5 by 2 cm., was seen. A biopsy was reported as lymphosarcoma, so a total gastric resection was done. The specimen showed diffuse lymphosarcoma, and a small ulcer was found in the fundus lying in the crevice between two large folds and was probably the source of the repeated hemorrhage. The patient was given radiation therapy and remained well for 18



Fig. 4a. Case 4. Annular narrowing of the prepyloric segment, with absence of peristalsis of the lesser curvature (July, 1952). b. Round filling defect of antrum (December, 1952), histologically a superficial spreading carcinoma with severe antral gastritis.

months but finally developed hepatomegaly, ascites and evidence of peritoneal spread. She died two years following the second operation.

Case 4. A 57 year old electrician had had rheumatoid arthritis for many years, and in January, 1952, was placed on Cortone, which relieved his joint pains. He was maintained asymptomatic on 50 mg, daily. In May he began to experience epigastric gnawing, which was relieved by antacids. On July 18 he became weak and fainted. Black, diarrheal stools were noted, so he was hospitalized. Bleeding continued for four days, during which time 3,000 c.c. blood were given. A gastro-intestinal series was reported as showing absence of peristalsis along the lesser curvature of the stomach, with annular narrowing of the prepyloric segment suggesting carcinoma of the antrum (figure 4a). Gastroscopy was not done. At operation the surgeon found the colon filled with altered blood. The stomach and duodenal bulb were described as completely normal on palpation and inspection and

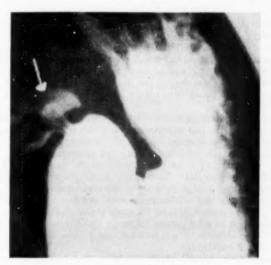


Fig. 5. Case 5. Niche in duodenal bulb indicated by the arrow. The contour of the bulb is not deformed.

were not opened. The small intestine was inspected carefully but no bleeding lesion was found. A cholecystectomy was done for gall-stones. It was believed that the hemorrhage had resulted from Cortone, although an ulcerating lesion was not discovered.

The patient was discharged feeling well but one month later complained of epigastric fullness, loss of weight, weakness and occasional "black stool," and he was thus referred here for study on December 22. Physical examination was essentially normal. Hemoglobin was 54 per cent; red blood cells were 3,400,000; stools contained 4 plus occult blood; gastric analysis was normal. Roentgenograms showed a small round filling defect in the prepyloric region (figure 4b) and an abnormal mucosal pattern of the antrum. Gastroscopy revealed a small nodular protrusion on the posterior wall of the antrum with large antral rugae, on the surface of which many hemorrhagic erosions were seen. The impression was carcinoma of the antrum, but antral gastritis could not be ruled out.

At laparotomy the gastric wall felt normal, but after prolonged palpation a small nodule was felt proximal to the pylorus. Despite the unimpressive finding a subtotal gastrectomy was done. The specimen showed a small sessile polyp, 5 by 5 mm., with coarse rugae in its vicinity and many superficial hemorrhages. The pathologic diagnosis proved to be superficial adenocarcinoma with severe antral gastritis. The

patient recovered uneventfully.

Case 5. A 41 year old male accountant had had a gastroenterostomy performed in 1925 at the age of 17 for bleeding duodenal ulcer. He remained well until 1935, when he suffered another hemorrhage but was not hospitalized. In 1943 hematemesis recurred and he was hospitalized, and roentgenograms revealed a niche in the duodenal bulb. The stoma was patent but barium left the stomach primarily through the pylorus. The patient was discharged on an ulcer diet which he followed rigidly, but nevertheless during the subsequent five years he experienced at least eight episodes of melena or hematemesis. In November, 1948, following hematemesis, roentgenograms revealed a normal gastroenterostomy stoma. The contour of the duodenal bulb was not deformed but a central niche was demonstrated (figure 5), and at four hours a large fleck of barium remained in the bulb, indicative of a large duodenal ulcer. Operation was performed two weeks later during a nonbleeding interval. The surgeon found the stomach and the duodenum normal on palpation and surface inspection. The stomach was opened and the stoma examined but no ulcer was seen. The duodenal bulb was opened but the ulcer seen on roentgenogram was not visible and no other source of hemorrhage found, so the abdomen was closed and the patient discharged.

Following the operation he noted mild epigastric pain, relieved slightly by milk and antacids, symptoms he had experienced for many years. On January 24, 1949, he was re-admitted to the hospital because of massive hematemesis, requiring numerous transfusions. Liver function studies and roentgenograms of the esophagus were normal. On February 8 he was referred to the author for study. Physical examination was not remarkable. Gastroscopy revealed a mild hypertrophic gastritis. Gastric analysis showed a high free acid. Roentgenograms showed the duodenal bulb deformed, probably due to the recent duodenotomy, and a central crater was again visible. It was indeed difficult to explain the roentgenogram demonstration of a niche in the light of a competent surgeon's inability to find one in the exposed duodenal floor. Nevertheless, it was believed that a subtotal gastric resection should

have been performed empirically.

One month later a subtotal gastric resection was done at a well known New England clinic and a duodenal ulcer was found in the resected specimen. There has been no further bleeding during the four years that have elapsed since the operation.

DISCUSSION

The inability to feel a comparatively large tumor through the stomach wall, to palpate a prepyloric carcinoma, or to identify an ulcer in the exposed floor of the duodenum—each is a surgical failure which is uncommon. However, they are hardly so rare as might be judged by the paucity of references to such occurrences in medical literature.

Findley, Kirsner and Palmer ¹ reported four cases of carcinoma of the stomach diagnosed correctly by roentgenogram or gastroscopy, yet at operation the lesion could not be identified and in three cases a second operation was required. Jankelson ² reported a case of repeated hemorrhage in which

the stomach was opened with negative findings, yet at post mortem a lymphosarcoma was found.

Errors of the type described in this presentation usually occur when operation is done after bleeding has stopped. They stem from several More than one lesion may be present, each of which may be a potential source of hemorrhage, and removal of one does not prevent recurrence of bleeding from the other. The commonest example of this, perhaps, is the recurrence of bleeding shortly after a subtotal gastrectomy for duodenal ulcer, where an undiscovered lesion was left behind in the gastric stump. Soft tumors, even though large, may not be palpable through the thick wall of the stomach, particularly in the cardia, where good exposure through an abdominal approach is not always possible. Thus in case 1 a hiatus hernia was readily found, while a large soft tumor in the immediate vicinity could not be felt by the surgeon; and in case 2 an antral gastritis attracted the surgeon's attention, while a carcinoma in a less accessible region could not be palpated. A superficial spreading carcinoma may be impalpable from the surface of the stomach, and even when the stomach is incised may be difficult to differentiate from gastritis.

There is no single or simple formula for the surgical management of cases of recurrent hemorrhage where roentgenogram and endoscopic studies are repeatedly normal. However, it would appear imperative that no roentgenogram or gastroscopic finding be ignored, regardless of the absence of a palpable pathologic lesion. Gastrotomy, duodenotomy and biopsy of mucosa which presented suspicious changes on roentgenogram or gastroscopy should be done in all cases where no obvious source for hemorrhage is found, since these procedures do not materially increase surgical mortality. The limitation of the surgeon's ability to detect pancreatic or biliary tract disease by palpation alone is well known, but its application to gastric disease has been less publicized.

Finally, just as the preoperative management of gastrointestinal bleeding requires the combined talents of the internist and surgeon, this teamwork may be extended to the operating room with advantage. Unfortunately, in the large majority of cases the internist responsible for the management of the patient during the diagnostic phase is rarely present at the operation, or at best attends as a silent bystander. It seems likely that if the gastrointestinal internist had attended the initial operations, more definitive surgical diagnostic measures to corroborate the preoperative diagnosis would have been instituted in cases 1, 2, 3 and 4, while in case 5 a subtotal gastrectomy would have been requested despite the inability to find a duodenal ulcer at laparotomy.

SUMMARY

Five cases of recurrent bleeding from the upper gastrointestinal tract are presented. The site and presumptive cause of hemorrhage were determined by roentgenogram or gastroscopy in each case preoperatively, yet at operation the surgeon was unable to corroborate the clinical diagnosis. In one case a hiatus hernia was repaired, in another antral gastritis was excised, while in three cases no cause for bleeding was found. Owing to recurrence of hemorrhage, a second operation was required in each case, at which time the original preoperative diagnoses were confirmed. In four cases a second operation would have been unnecessary had the stomach been opened for inspection at the site where pathologic changes had been noted on roent-genogram or gastroscopy.

Conclusion

Palpation and inspection of the stomach at operation may be unreliable. Roentgenologic and gastroscopic findings should be substantiated, if necessary, by opening the stomach.

BIBLIOGRAPHY

- Findley, J. W., Jr., Kirsner, J. B., and Palmer, W. L.: Gastric cancer: difficulties in recognition at laparotomy, Gastroenterology 14: 502-508 (April) 1950.
- Jankelson, I. R., and Milner, L. R.: Massive upper digestive tract hemorrhage of undetermined origin, J. A. M. A. 145: 17-21 (Jan. 6) 1951.

RHEUMATISM AND ARTHRITIS

REVIEW OF AMERICAN AND ENGLISH LITERATURE OF RECENT YEARS

(TENTH RHEUMATISM REVIEW) *

Part II

By WILLIAM D. ROBINSON, M.D., F.A.C.P., Ann Arbor, Michigan (Chairman, Editorial Committee), EDWARD W. BOLAND, M.D., F.A.C.P., Los Angeles, California, JOSEPH J. BUNIM, M.D., F.A.C.P., Bethesda, Maryland, DARRELL C. CRAIN, M.D., F.A.C.P., Washington, D. C., EPHRAIM P. ENGLEMAN, M.D., F.A.C.P., San Francisco, California, WALLACE GRAHAM, M.D., F.R.C.P. (C), Toronto, Canada, L. MAXWELL LOCKIE, M.D., F.A.C.P., Buffalo, N. Y., MAX M. MONTGOMERY, M.D., F.A.C.P., Chicago, Illinois, CHARLES RAGAN, M.D., F.A.C.P., New York, N. Y., MARIAN W. ROPES, M.D., F.A.C.P., Boston, Massachusetts,

CONTENTS

EDWARD F. ROSENBERG, M.D., F.A.C.P., Chicago, Illinois, and

CHARLEY J. SMYTH, M.D., Denver, Colorado

PART II

2 11113 22	
"Collagen Diseases"	758
Psoriatic Arthritis	767
Reiter's Syndrome	768
Neuropathic Arthropathies	770
Epidemic Tropical Acute Polyarthritis	772
Hemophilic Arthritis	772
Rheumatic Purpura	773
Palindromic Rheumatism	773
Allergic Arthritis	775
Pharmaceutic Arthritis	
Alkaptonuria and Ochronosis	778
	780
Reflex Sympathetic Dystrophy	782
Brachialgia	784
Nonarticular Rheumatism	785
Tumors of Synovia	796
Arthritis Related to Primary Bone Disease	798
	803
Structure and Function of Articular Tissues	804
Experimental Arthritis	810
	812

^{*} Received for publication May 22, 1953.

Part I of this Review appeared in the preceding issue of this Journal.

This Review was prepared by the Editorial Committee of the American Rheumatism Association. The editorial comments express the opinions of the authors of the Review, the Editorial Committee, not necessarily those of the Association.

THE "COLLAGEN DISEASES"

Several diseases of unknown etiology have been grouped together because of clinical similarities, similar sites of pathologic involvement, and a possible common pathogenesis. The group known as "the collagen diseases" has included rheumatic fever, rheumatoid arthritis, periarteritis nodosa, lupus erythematosus disseminatus, scleroderma, dermatomyositis and possibly malignant nephrosclerosis. A brief explanation of the manner in which this grouping came about and the inaccuracies in terminology involved is necessary for an adequate discussion of the literature.

In 1932, Klinge and Grzimek originated a concept based on similarities between the lesions observed in certain of these diseases—rheumatic fever and periarteritis nodosa particularly-and those seen in animals subjected to sensitization with a heterologous protein. Rich 1674 has continued to favor this approach and has observed periarteritis nodosa in patients exhibiting sensitization, particularly to the sulfonamide drugs. Sensitization to vaccine has been described also in patients with lupus erythematosus disseminatus.62 In most instances, however. no obvious antigen has been found, and a recognizable sensitization pattern has not been apparent except in rheumatic fever. There are unexplained individual variations in host reactivity to sensitizing agents within and between species. 1674 Klemperer 1112, 1113 adopted the name "collagen diseases" and grouped the diseases upon the basis of morphologic similarities, but has not gone as far as Rich, 1674 who suggested the common etiologic basis of sensitization. Klemperer 1113 pointed out that one so-called typical feature, that of the fibrinoid change, is nonspecific and can be produced where no element of sensitization exists, as in the base of a peptic ulcer or following simple trauma. Duff 463 noted three phases of the reaction of this tissue to insults-destructive, proliferative and inflammatory—which vary in degree and in anatomic location to make up the pathologic picture of each of the diseases in the group. The wide distribution of fibrous connective tissue and its potential involvement at any site probably account for the diversity of clinical manifestations seen in these diseases.

Since fragmentation of collagen is seen when tissues from these diseases are studied with the light microscope, Duff 463 has favored the term "collagen diseases." Klemperer used the term collagen in the sense of the German school of the early twentieth century, whereby all extracellular components of the connective tissue are called collagen.1113 He has viewed this group of diseases as characterized anatomically by a generalized alteration in the connective tissue, particularly in the ground substance. Indirect evidence has accumulated indicating that the primary change takes place in the ground substance between the collagen fibers and fibrils. Altshuler and Angevine 31 suggested that the fibrinoid change may be related to changes in the ground substance, but there has not been unanimity on this point. [Fibrinoid change may result from deposition upon the connective tissue of material derived from the blood.-Ed.] If the change in collagen or ground substance is the result of sensitization, the antigen involved is unknown. Most collagen is insoluble, and Waksman and Mason 2104 were unable to make particulate collagen antigenic. Purified fractions of the ground substance also have shown no antigenicity. [In the last decade, ability to define collagen has advanced rapidly and we now have the histologist's definition of the substances as seen through the light microscope, the biochemist's definition and, finally, that of observers using the electron microscope and x-ray diffraction technics. Recent studies using x-ray diffraction and special chemical analyses indicate that apparently normal collagen exists in the

rheumatoid nodule beside areas where collagen is absent. The fibrinoid change appears to be most frequently associated with absence of collagen. Evidence that the primary focus lies in the ground substance remains indirect, is unsatisfactory, and requires much more clarification before achieving wide and complete acceptance. Some prefer the term "connective tissue disease," which avoids implications as to which component of the tissue is primarily involved.—Ed.]

The diseases in this group have certain clinical similarities, since in many of them particular structures and blood vessel walls are involved.^{317, 1027} Numerous case reports have appeared ^{103, 217, 416, 1289, 1733, 1954, 2247} in which one member of this disease group appears where another was suspected, or where lesions of two or more of these diseases have been found in one individual. [This probably reflects our frequent inability to make a correct antemortem diagnosis in this obscure group of diseases, as well as the limited ability of the tissues involved to react to

insult. It does not necessarily prove a common etiology.-Ed.]

Many others have considered the clinical and pathologic differences and similarities among these diseases. ^{68, 1027, 2039} The evidence favoring vascular allergy in the pathogenesis was reviewed, ¹³⁸⁷ and the term "visceral angiitis" was introduced to designate the alleged common pathologic denominator, especially in disseminated lupus and periarteritis. ^{165, 1385} Baehr and Pollack ⁶⁸ emphasized the differences among the various conditions included in this group, and concluded that "fibrinoid degeneration is not a pathologic process of sufficient specificity to serve as a reliable common denominator for the classification of disease," and that acceptance of an allergic basis for these diseases "without other supporting evidence serves merely to discourage other avenues of investigation into their essential nature."

[The views of Klemperer by which no etiologic similarity is implied in the act of grouping these diseases together seems the safer course, since a common etiology, although possible, remains unproved, particularly when one realizes that the tissue involved is a simple one with limited capabilities in its reaction to injury. 68, 468, 1112 The term "collagen diseases" serves a useful purpose at the present, but should be regarded as temporary, subject to revision as our knowledge advances.—Ed.]

Lupus Erythematosus Disseminatus (L.E.D.)

This systemic disease was the subject of considerable interest. Although a relationship to discoid lupus erythematosus was not recognized by some, ⁵⁴ others stated that chronic discoid lupus may convert to the subacute or acute form at any time. ²¹⁷⁵ The cutaneous pathology of chronic discoid and disseminated lupus appeared to be quantitatively the same. ¹³⁴⁰ The differentiation between acute and subacute lupus depended upon the rapidity of onset and the severity of involvement.

Clinical Features. The literature substantiated the accepted clinical features of erythematous skin lesions; constitutional symptoms of cachexia, fever and weight loss, arthralgia and arthritis; suppression of blood-forming elements, with leukopenia, secondary anemia and thrombopenia; adenopathy; nonbacterial endocarditis; polyserositis with pleurisy; pericarditis and ascites; renal disease; and a higher incidence in females.

Reviews 277, 690, 1418, 1518, 1787, 2075 and a host of case reports indicated that the disease continued to occur predominantly in women. The peak incidence fell between

10 and 40 years of age, 1467, 2075 with the onset of the acute form usually somewhat earlier. 1418 The disease occurred in members of the dark-skinned races. 130, 277, 1880, 2075, 2094 Sensitivity to sunlight sometimes was temporarily related to the disease onset. 1307, 1418 The duration of the disease averaged four years and four months in one series, 2075 but varied from rapid fatality within 16 days of onset 1444a to a prolonged course, with patients alive and in remission after 10 to 15 years. 1459, 2075

The incidence of skin lesions at some time during the course of the disease remained high, 1418, 2075 but skin and mucous membrane lesions were totally absent in some instances. 210, 277 Alopecia was observed repeatedly. 924, 1508, 2250 Arthralgia or polyarthritis, 62, 277, 389, 924, 1418, 1459, 1513, 2075 and polyserositis with effusions 277 in the form of pleuritis, 62, 951, 1580, 2075, 2187 or pericarditis 380, 389, 951, 1580, 1508, 2075 were noted repeatedly. Peritonitis 2073 was seen with less frequency. Transient pneumonitis was not infrequent, 567, 1307, 2075 Generalized adenopathy was noted in approximately half the patients. 277, 2075 Hypertension occurred infrequently. 389 Involvement of the heart was manifested by cardiac enlargement, 1307 a variety of murmurs 389, 951, 1598 and pericardial friction rubs, 951 These findings were correlated at autopsy with mural endocarditis 62, 210 and pericarditis with effusion. 251 Local vasomotor disturbances were conspicuous in some instances, 251 with a characteristic erythema of the finger tips 1513 and Raynaud's phenomena. 390

Various eye ground changes were described. 353, 2098 They were not specific, but were significant in the absence of hypertension. 2075 Neurologic manifestations of acute and subacute L.E.D. included toxic psychosis, neuronitis, focal central nervous system lesions, cerebral hemorrhage with thrombocytopenia, and Sydenham's chorea. 1796 Convulsions were sometimes a terminal event. 130, 380 In other patients generalized convulsions, toxic psychoses, transient coma, hemiplegias, transient bilateral ptosis, and Jacksonian convulsions occurred. 2075 Thrombocytopenic purpura has appeared as

the presenting symptom. 204, 277

Pathology. The pathologic findings in L.E.D. were described in numerous papers. ^{103, 130, 287, 353, 389, 463, 851, 1112, 1236, 1307, 1418, 2040, 2075, 2094} In one series the characteristic lesion with fibrinoid necrosis of the connective tissue was present in the pericardium in 70 per cent, in the endocardium (Libman-Sacks vegetations) in 55 per cent, in the myocardium in 35 per cent; in the kidneys as wireloops in 60 per cent, as focal loop necrosis in 85 per cent, as vascular lesions in 40 per cent; in vessels and other sites in 65 per cent, and in the spleen in 95 per cent. ¹¹¹² Identical changes in joint capsules were also described. ^{130, 1112} In other series the wire-loop lesions of the kidney were uncommon. ¹⁴¹⁸ In a group of patients with arthritis, albuminuria, nephrotic edema and renal insufficiency, the kidneys at autopsy were found to be large and pale (the basic lesion being proliferation of endothelial cells of the capillaries, causing obstruction of the capillary loops), giving a picture of subacute glomerulonephritis. Typical lesions of L.E.D. were also found. ^{210, 380}

The histologic changes in the skin lesions were reviewed.^{130, 1418} Alteration of collagen, including fibrinoid changes in the walls of the vessels of the skin, occurred in less than one fourth of the cases.¹⁴¹⁸ Skin biopsy, however, sometimes proved useful in diagnosis.²⁷⁷ A chronic inflammatory lesion was found in the muscles of patients with this disease, especially in those who had joint symptoms.¹⁹⁵⁰ It was indistinguishable from similar lesions found in a variety of other diseases.^{1277, 1498} Several types of microscopic ocular lesions were described in acute L.E.D., none of which could be considered pathognomonic.²⁸⁸

Hematoxylin-stained bodies were noted in the tissues of lupus patients, but were not found in other diseases. 721, 1116, 1118 They were present most commonly in the

kidneys and endocardium, but were also found in other tissues of mesenchymal origin. These bodies varied in size from a cell fragment to almost macroscopic proportions, and their derivation could be traced from the nuclei of cells of mesenchymal origin; they appeared to have been phagocytosed both by polymorphonuclear leukocytes and by histocytes. By histochemical methods, the material was identified as depolymerized desoxyribose nucleic acid, similar to that found in the L-E cell.¹¹¹⁸

Cases of clinically typical acute L.E.D. were again described in which autopsy revealed no lesion to substantiate the diagnosis or explain the clinical picture. 690

Laboratory Findings. Albuminuria and abnormal urinary sediments were seen in a high percentage of cases.^{277, 1418, 2075} Leukopenia was present in four fifths of patients with the acute disease ^{1418, 1513} and in two thirds of those with the subacute form.¹⁴¹⁸ Thrombocytopenia was seen repeatedly.^{204, 277, 1513, 2075} Partial or complete disappearance of eosinophils from the peripheral blood was noted.^{534, 2058}

Reversal of the albumin/globulin ratio was seen often in both the acute forms ⁸⁶¹, ¹⁴¹⁸, ¹⁵¹⁸ and the subacute forms, ¹⁴¹⁸ usually associated with a globulin elevation. ²⁷⁷, ²⁰⁷⁵ The electrophoretic pattern of serum proteins may be characteristic in patients with L.E.D. ¹⁰³, ¹⁶⁶⁵ While the total protein was at times within normal limits, the albumin fraction was decreased and the alpha₂ and gamma globulin fractions were increased, in some instances constituting 50 per cent of the total protein. Following therapy with cortisone or ACTH, the gamma globulin decreased and the albumin increased, but the alpha₂ globulin remained unchanged. Associated with these changes, cephalin floculation, thymol turbidity ¹²¹⁸ and serologic tests for syphilis ¹⁴¹⁸, ¹⁶¹³, ¹⁶⁶³ were sometimes positive in both subacute and acute L.E.D.

Nonspecific electrocardiographic abnormalities were described, 951, 1220 although the electrocardiogram was within normal limits in three patients with abnormal cardiac findings at post mortem. Specific strains of streptococci were incriminated in the pathogenesis of L.E.D. (and other diseases) by one investigator, 2184 who proposed a

diagnostic test based on this finding.2188

The "L-E Cell." Of major diagnostic importance has been the discovery and clinical application of the phenomenon known as the "L-E cell," first described in bone marrow material by Hargraves, Richmond and Morton. 781, 819 The phenomenon was believed to result from the phagocytosis of free nuclear material by a mature polymorphonuclear leukocyte, or from autolysis of one or more nuclear lobes within a mature polymorphonuclear leukocyte. The reaction was noted to be more frequent and more prominent with increasing severity of the disease. 780 Subsequently, the cell was seen in oxalated venous blood of patients with L.E.D.. 1990 and the agglutination of the nuclear material with clusters of polymorphonuclear leukocytes (rosettes) was described. The phenomenon could be produced when marrow or the defibrinated buffy coat from a normal individual was incubated with plasma from a patient with L.E.D.94 The phenomenon was seen in clotted blood, 95, 667 and could be produced with plasma from cases in which the L-E cell was not found in the bone marrow. 780 The phagocytosed material in the L-E cells was identified as depolymerized desoxyribose nucleic acid. 731, 1114 Following treatment of patients with cortisone or ACTH, a decrease in the number of rosettes and of L-E cells was observed. 1508 Several variants of this test for L-E cells were described, depending on the interaction of cells from a buffy coat of peripheral blood or bone marrow (human or animal) and the plasma of a patient with L.E.D. 137, 780, 1414

The material responsible for the production of the rosettes and the L-E phenomenon was found to be in the gamma globulin fraction. 197, 818 It was stable if

kept sterile, and was destroyed at 65° C.; it was inhibited by PABA and its specific rabbit antiserum, ⁸¹⁴ but not by a variety of hormones in vivo nor by the in vitro addition of cortisone. ⁶⁶⁷ Rabbits immunized with gamma globulin isolated from L-E plasma formed a specific antibody to the L-E factor, which differed immunologically from the antibody to normal human gamma globulin. ⁸¹⁷ L-E cells have been produced in the skin of human volunteers following the inoculation of experimental windows with the plasma of a patient with acute L.E.D. ¹⁶⁴⁰

The L-E cell has not been found in patients with dermatomyositis, numerous instances of leukopenia, chronic discoid lupus erythematosus, ⁸¹⁹ cirrhosis, scleroderma or rheumatoid arthritis, or in normal individuals. ^{277, 815} Isolated false-positive L-E preparations have been reported in multiple myeloma, ¹⁴¹⁸ leukemia, ⁵⁵⁵ pernicious anemia, dermatitis herpetiformis, chronic discoid lupus erythematosus, and in three patients with an unknown diagnosis. ¹³⁷ The presence of the L-E cell has been almost specific for active L.E.D., ^{780, 781} and has been noted in many reports. ^{94, 95, 277, 780, 781, 814, 815, 816, 1277, 1598} It was seen in about 25 per cent of patients with subacute L.E.D. ⁹⁵ [While its exact place in the diagnosis of L.E.D. is not yet clear, the finding of a positive L-E preparation is presumptive evidence of L.E.D.; a negative test does not rule out the disease.—Ed.]

Treatment. Many reports appeared on the use of corticotropin (ACTH) 407, 524, 688, 811, 1580, 2056, 2057, 2160 and cortisone. 69, 70, 241, 277, 1348, 1800 Dosages of corticotropin needed for prompt clinical improvement varied from 150 mg. a day 69, 688 to 20 mg, a day. 534 The daily dosage of cortisone was between 150 and 200 mg. intramuscularly, and the daily requirement of either hormone in L.E.D. was considered to be higher than in rheumatoid arthritis.241, 1348 Prompt improvement in the clinical condition of the patient was usually noted. Within 24 to 48 hours, there were increase in strength, amelioration of arthralgia and defervescence. The skin rash tended to disappear by the tenth day. Less consistent effects were noted on leukopenia, sedimentation rate or L-E cell test. Following discontinuation of therapy, patients relapsed within a few days to several months. In most reports the period of treatment was very short, five to 10 days. In some, treatment was continued from four to six weeks. The length of treatment did not seem to influence the rapidity of relapse. As in other diseases treated with corticotropin or cortisone, untoward physiologic effects were noted, including psychotic aberrations. The possibility that these episodes may be related to the underlying process of L.E.D. in the central nervous system was considered. 70, 241, 277

Tocopherol (vitamin E)²⁵⁸ and para-aminobenzoic acid ²²⁴⁶ were not of value in acute L.E.D., and the earlier reports of their effectiveness in more chronic forms of the disease were not substantiated.^{563, 1764} The administration of pantherol, the alcohol of pantothenic acid, was followed by improvement in only two of nine patients with acute L.E.D.; results were better in the subacute and discoid forms.⁶⁶³ Isolated good results ^{1432, 1975} and poor results ⁹⁹⁶ were obtained with penicillin. A patient with severe thrombocytopenic purpura complicating L.E.D. who was subjected to splenectomy experienced remission for at least one year.²⁰⁴ An unsuccessful attempt was made to ameliorate the hypertension of a patient with L.E.D. by splanchnicectomy.⁹²⁴

Periarteritis Nodosa (P.A.N.)

Periarteritis nodosa (P.A.N.) is a disease with protean manifestations in which medium and small sized arteries are involved in an inflammatory process.

Clinical Features. Because of the multiple and variable involvement of different organs, the clinical features of P.A.N. are frequently bizarre and not readily explainable by a single diagnosis. The disease is usually manifested by fever, malaise, anorexia, fatigue, and symptoms and signs referable to the organs involved. The incidence of certain clinical features in 30 patients with proved P.A.N. was: hypertension, 67 per cent; fever, 70 per cent; gastrointestinal symptoms, 79 per cent; peripheral neuritis, 73 per cent; renal involvement, 50 per cent; cardiac disease, 51 per cent; skin and subcutaneous tissue involvement, 43 per cent; and skeletal muscle lesions, 40 per cent. In recent years, many review articles concerning the disease have appeared. In recent years, many review articles concerning the disease have appeared. The average age is about 40, although the typical disease has been seen in children. The average age is about 40, although the typical disease has been seen in children. The ratio of male patients to female ranged from 3:1 to 10:1. The prognosis depends on the organs involved. Survival periods of less than six months, The prognosis depends on the organs involved. Survival periods of less than six months, The prognosis depends on the organs involved. Survival periods of less than six months, The prognosis depends on the organs involved.

In 30 patients with proved disease, 89 per cent showed abnormal urinary findings and 69 per cent had hypertension. 1635 Two types of renal change were described: severe glomerular involvement without occlusive vascular changes, and occlusive vascular changes without glomerular involvement. 606 Individuals with occlusive involvement of large renal arteries and minimal glomerular disease usually were hypertensive, but hypertension without renal involvement was reported. Gastrointestinal lesions resulted from infarcts and hemorrhages secondary to arterial disease.248, 1810, 1278, 2199 Central nervous system lesions 1811, 1972, 1989, 2191 and peripheral neuritis secondary to arteritis of the vasonervorum were again described. 1242, 1526 The neuritis affects motor nerves most commonly and may regress, recur or remain as a sequel to the disease. It was impossible clinically to differentiate the neuritis from that due to other causes without considering the total clinical picture. Pulmonary vascular lesions were associated with parenchymal involvement,2005 and it was believed that Loeffler's syndrome may represent a mild variant of pulmonary arteritis. A rare phenomenon of pulmonary cavitation due to polyarteritis was reported. Skin and subcutaneous involvement with nodular lesions resulted from aneurysmal dilation of involved subcutaneous arteries and from hemorrhagic dermal lesions. 1462, 2024 The bizarre nature of this disease was illustrated in many case reports.

Pathology. There was general agreement concerning the pathologic changes. 463, 1100, 1111, 1113, 1674, 2235, 2251 Lesions are found in medium and small sized arteries throughout the body, at times with one segment of a vessel diseased and the adjacent area unaffected. The process may involve the entire circumference or only a small part of the vessel wall. The acute lesion is one of edema of the media and perivascular areas, followed by inflammatory exudation into the perivascular tissue with polymorphonuclear and eosinophilic leukocytes. Later there is fibrinoid and hyaline degeneration of connective tissue in the vessel wall. In the reparative process, fibrosis occurs most densely in the adventitia, but is found throughout the wall. The end stage results either in occlusion of a vessel, with resultant infarction, or in weakening of a segment of the wall, producing an aneurysm which may rupture. Lesions of the acute, late or healed stages were found in the same individual and, at times, in the same vessel. Some distinguished "hypersensitivity angiitis" from typical P.A.N. on the basis of morphology and location of lesions. 2251

Etiology. At present, the disease must be considered to be of unknown etiology, although there is real similarity between periarteritis nodosa and the manifestations of sensitization, as, for example, to foreign protein.^{714, 1674} Initiation of the disease followed clinically evident sensitization to poison oak and primrose, ¹⁷⁴⁷ propylthiouracil, ¹⁸⁸⁷ dilantin sodium, ²⁰⁸⁹ and the parasite *Trichinella spiralis*, ¹⁴⁴⁸ It coincided with rat-bite fever ¹⁶⁰² and scarlet fever, ¹⁵⁴⁴ and was associated with or followed postvaccinal (yellow fever) hepatitis. ¹⁵⁴² Additional cases were noted to follow sulfonamide administration, ^{672, 1218} and the apparent increased incidence of this disease since 1936 was again attributed to the introduction of these drugs, ^{417, 629} From 1916 to 1935, P.A.N. was encountered in only six of 10,036 autopsies at the Johns Hopkins Hospital; from 1936 through 1944, 32 cases were found in 4,483 autopsies. ¹⁶⁷⁴

Rich reviewed his extensive experimental work in a Harvey lecture. 1674 The production of arterial lesions by protracted anaphylactic reactions was confirmed by some 821, 923 but not by others, 27, 1862 [In experiments with large numbers of animals, only a portion developed lesions; apparently these changes cannot be produced uniformly at will. Ed.1 The histologic picture of P.A.N., stated to resemble the human disease more closely than that produced by hypersensitivity, developed in unilaterally nephrectomized rats after the remaining kidney was enclosed in silk. 1100, 1862, 2251 Development of lesions was attributed to sharply rising hypertension 2251 and to infection. 1100, 2251 Periarteritic lesions were induced in rats by production of an "endocrine kidney"; the incidence and severity of the lesions were not influenced by dietary intake of salt or protein, 1808, 1809 Selve continued to regard P.A.N. as a disease of adaptation. 1804 In view of similarities between the fibrinoid and fibroblastic changes in placental arteries and the vascular changes in P.A.N., it was suggested that P.A.N. and all "collagen" diseases may represent an abnormal acceleration of the aging process.2235 [The evidence for a hypersensitivity mechanism in the pathogenesis of P.A.N. seems more impressive than in other "collagen diseases," with the possible exception of rheumatic fever.-Ed.]

Laboratory Findings. Laboratory findings in P.A.N. are notable for their variability. Wold and Barker 2199 described anemia in 60 per cent of patients, leukocytosis in 80 per cent, eosinophilia in 17 per cent (usually associated with asthma), markedly elevated erythrocyte sedimentation rate in 100 per cent and azotemia in 50 per cent. In one patient the picture simulated that of eosinophilic leukemia, with an eosinophilia of 75 to 90 per cent. S A urinary sediment which "telescoped" simultaneously the findings seen in all stages of glomerulotubular nephritis was considered characteristic of both P.A.N. and L.E.D. 203, 1385 A protein which precipitates in the cold and does not redissolve on returning to room temperature was found in the sera of patients with P.A.N., as well as in other diseases with hypergammaglobulinemia. 1194

Histologic examination remains the means of establishing a positive diagnosis. "Blind" muscular biopsy was positive in only one third of the patients.²¹⁹⁹

Treatment. No specific therapy is available for P.A.N. Experimental arterial lesions resulting from sensitization have been decreased in number and severity by the administration of salicylates, 1873, 1987 but the effects of salicylates in the human disease have not been remarkable. Antihistaminics have been of no value. 1998 The administration of cortisone and corticotropin to rabbits during sensitization to horse serum was followed by a decrease in the incidence of arterial lesions. 142, 1975 Eight patients with P.A.N. treated with cortisone or corticotropin noted prompt relief, but relapse occurred following cessation of therapy. 684, 1824, 2057 Pathologic specimens from two patients who died after initial improve-

ment showed healing of all arterial lesions, but widespread visceral infarction from fibrous obliteration of vessels.1824

Dermatomyositis

Dermatomyositis is an obscure and poorly defined syndrome involving the skin, skeletal muscles and many organs.²¹⁰² Although usually chronic in nature, it may have an acute course.²⁰⁰, ¹⁰⁰¹

Clinical Features. The systemic symptoms of dermatomyositis are often unimpressive and vague: loss of weight, general malaise, low grade fever, vasomotor disturbances of the Raynaud type, muscular aching, and arthralgia may be seen. Less frequent are gastrointestinal manifestations such as dysphagia 448, 1214, 1226, 2012 and vomiting. 1835, 2102 Hypertrichosis may follow an exacerbation of the cutaneous lesions. Diplopia may occur during the course of the disease. 1503, 1622

Carcinoma was frequently found to be associated with dermatomyositis. 448.

Striated muscles, particularly in the upper extremities ²²² and the skin, are the most frequently involved tissues. ¹⁸³⁵ Aches and pains, ²¹⁸⁶ swelling, tenderness on pressure, ⁴⁴⁸ and eventual atrophy ¹⁶⁵⁶ are common manifestations of muscular involvement. Muscular degeneration may result in fixation of the joints, flexion contractures and crippling. ^{222, 1503, 1835} Weakness of sphincters as well as of facial muscles was often noted, although the latter was less common than in myasthenia gravis. ¹⁸⁰³ The cutaneous lesions in dermatomyositis are inconstant and variable. ^{1409, 1808} Skin lesions were described that started on the extremities, gradually involved the trunk and face and were aggravated by exposure to ultraviolet light. ²¹⁸⁶ A butterfly pattern closely resembling that of L.E.D. may occur. ²²² Cutaneous edema of the involved parts, ²¹⁰² diffuse calcium infiltration of the skin, ^{1363, 1486} and telangiectasis and atrophy ⁴⁴⁸ are rare manifestations.

Pathology. The cutaneous, muscular and visceral lesions in dermatomyositis are not specific. 448, 1277, 1409 Degeneration of muscle and of collagen was thought to represent the basic morphologic alteration. 222 The cutaneous changes are of a benign inflammatory character associated with mild acanthosis or atrophy. 1803 Inflammation was thought by some to constitute the first phase of the various alterations, 1803 but others felt that the inflammatory process is secondary to muscle degeneration. 2102 Fibrous replacement may appear, 1803 and may become extensive in long-standing disease. 222 Nonspecific lesions consisting of interstitial edema, foci of degeneration and inflammation and eventually fibrosis were encountered in various organs. Thromboses with congestion and hemorrhage followed involvement of blood vessels, 1520, 1835, 2102 Nonspecific changes in the retina were described. 1227 Since the muscles in the shoulder girdle are often involved, biopsy of the pectoralis major may be of diagnostic help. 1803

Etiology. The etiology remains obscure. Infection, 222, 1656 more specifically a streptococcal infection, 1691 and sensitization of the skin and muscles to some bacterial product were suggested. 913, 1891 In some fashion, malignancy may play a rôle in pathogenesis. 1835

Laboratory Findings. Creatinuria of an abnormal degree was observed, 1803, 1856, 2249 sometimes appearing early in the course of severe extensive disease, 1214, 1486, 1503, 1856, 2186 Eosinophilia was frequent, 222, 1214, 1503, 1856, 2186 and the sedimentation rate was often moderately elevated. 1803, 2186 Less frequent were leukocytosis 1856 and elevation in the antistreptolysin titer. No specific electrocardiographic or roentgen-

ologic changes were observed.²⁰¹² The affected muscles in dermatomyositis responded to both faradic and galvanic currents without a reaction of degeneration, although a 25 to 40 per cent increase in strength of current was required to cause contraction.²²²

Treatment. The therapy of dermatomyositis remained largely symptomatic. Adequate nursing care and physiotherapy were recommended.^{222, 1480, 1503} Testosterone propionate in conjunction with amino acids and vitamins, ¹¹⁰⁴ para-aminobenzoic acid associated with physiotherapy, ²²⁴⁹ and penicillin ³⁰⁹ were occasionally used with success. More recently ACTH and cortisone were administered to a limited number of patients for short periods of time, with varying success. ^{494, 1246, 1507, 1622, 2057}

Scleroderma

Knowledge of scleroderma extends only to the descriptive phase, and understanding of the disease remains superficial. Collagenous connective tissues of the skin and subcutaneous elements are not exclusively affected, but the process may be widespread and involve virtually all the tissues of the body. 68

Clinical Features. Skin Involvement. The cutaneous changes in scleroderma are characterized by a waxy edematous induration, frequently associated with Raynaud's phenomena 1228, 1738, 1740, 1857 and, less frequently, with arthralgia. The uncommon association of diffuse scleroderma with calcinosis was referred to as the Thibierge-Weissenbach syndrome. The Alteration of the skin may begin on the extremities or at the bridge of the nose and cheeks; eventually the cutaneous manifestations may extend slowly to involve the whole face, the extremities and the trunk.

Visceral Involvement. The protean nature of the noncutaneous manifestations of scleroderma was illustrated by a patient in whom, over a period of 19 years, the diagnoses of Addison's disease, chronic ulcerative colitis, heart disease, carcinoma of the stomach and pulmonary tuberculosis were made before scleroderma was finally diagnosed.86 The many visceral manifestations of the disease were reviewed.119 In the gastrointestinal tract, the esophagus was most frequently involved. 195, 209, 582, 1214, 1838, 1619, 1783 Lesions of the gastrointestinal tract are not specific 1857 but can cause death,1261 Involvement of the lungs with fibrosis alone or associated with a cystic process was described, 56, 307, 447, 582, 1228, 1892, 2166 and may occur in the absence of obvious skin changes.307 The heart can be involved to the extent of complete heart block and death from heart failure. 471, 1821 Jacksonian convulsions developed in a patient with generalized scleroderma. Tab A dental feature was widening of the peridontal space, particularly of the molars, with or without loosening of the teeth.1788 Partial disappearance of the lamina dura was also seen.1134 The disease has produced facial hemiatrophy with ankylosis of the temporomandibular joint. 1732 Generalized scleroderma has been associated with bilateral cataract as well as with less serious eye and ear conditions.110 No close relationship with neoplasia, such as that described in dermatomyositis, has been observed in scleroderma.

Pathology. Although areas of fibrinoid degeneration may be seen in the skin, the predominant change is a diffuse sclerosis of the intradermal and subcutaneous connective tissue.⁶⁸ Intimal fibrosis, edema, venous myomatous proliferation ¹²⁶¹ and fibrinoid degeneration in the walls of small arteries ⁶⁸ were frequently found in generalized scleroderma. Baehr and Pollack considered the pathologic changes seen in diffuse scleroderma in the arteries, in the endocardial and subendocardial connective tissue, and in the glomeruli to be identical with those which they had described for L.E.D., including the "wire loop" lesions and focal necrosis of glomerular tufts.⁶⁸

In the lungs, scleroderma produced compact pulmonary scierosis without dissolution of lung tissue 1892 or replacement of parenchyma by bronchiolar proliferative tissue which was subject to progressive cystic distention. 447 In the heart, focal areas of fibrotic scarring without much cellular infiltration or vascular change were distributed throughout the myocardium. 471, 1821

Etiology. The etiology is unknown. Infection, alteration in protein metabolism, ³²⁰ sensitization phenomena ^{1856, 2108} and genetic faults have been suggested as possible causes of the disease. Acid-fast bacilli were found in sputum, blood, or nasal or subcutaneous tissue smears in five cases. ²²⁸⁰

Laboratory Findings. Laboratory procedures are of little help in diagnosis. Hypoalbuminemia with hypergammaglobulinemia ²¹⁰⁸ and increased creatinuria ⁴⁷¹ have been observed. Roentgen appearance of the gastrointestinal tract may suggest

the possibility of scleroderma. 1039, 1738, 1770

Treatment. No therapy capable of consistently modifying the slow downward course of generalized scleroderma has been found. General supportive measures and physical therapy were widely recommended. 120, 415, 1738 Drugs advocated have included bismuth, 1878a methyltestosterone, 1321 vitamin D, 1485, 1504 procaine hydrochloride, 2076 Promin, 2230 crude fermentation concentrate rich in B₁₂, 60 and para-aminobenzoic acid. 1749, 2249 The results with corticotropin and cortisone in small series of patients have been equivocal. Although with both hormones a transient amelioration in the signs and symptoms of scleroderma has resulted, 116, 1348, 2057 the fundamental course of the disease has not been altered. 2087

PSORIATIC ARTHRITIS

With few exceptions, 1980 the association between psoriasis and arthritis of the rheumatoid type was considered significant. In 10,000 medical patients, psoriasis was found in 0.43 per cent; among 1,000 patients with rheumatoid arthritis, psoriasis was found in 3.1 per cent. 2129 In another series of 930 patients with rheumatoid arthritis, 53 patients (5.6 per cent) had psoriasis. 298

Proof is still lacking that psoriatic arthritis is a specific entity. 1579 Restriction of the term to arthritic changes in the terminal interphalangeal joints was criticized. Inclusion of patients with psoriasis and rheumatoid arthritis who exhibit striking correlation of remission and exacerbations of the skin and joint manifestations was advocated. 1579 Cecil 288 regarded it as "just a matter of accident whether it involves the terminal phalangeal joints or not." Accepted criteria for psoriatic arthritis would exclude cases for which coincidence is not a satisfying explanation. The standpoint of roentgenology, the impression was gained that often when the joints are the primary target tissue, with psoriasis following later, the articular changes tend to be indistinguishable from those in rheumatoid arthritis, whereas in patients with psoriasis of long standing in whom arthritis occurs later, there tends to be a somewhat distinctive radiologic appearance. 828

Clinical Data. In 31 of 53 cases the psoriasis developed before the arthritis, in six it appeared after the arthritis and in 10 both diseases seemed to develop at about the same time.²⁹⁸ [Apparently onset was not ascertained in the remaining 6 cases.—Ed.] In a patient with arthritis mutilans the joint lesions preceded the psoriasis by eight years. When the arthritis became quiescent after five years, the fingers had shortened to "mere bags of useless flesh." The psoriasis did not start until two years later.⁸¹² In another patient, involvement of terminal joints was not predominant. But there were destructive lesions of the midphalangeal and metatarsophalangeal joints of the toes which were not characteristic of rheumatoid arthritis.¹¹⁶⁸ In a patient with Felty's syndrome, psoriasis developed for the first time four years after splenectomy.¹⁰⁸

Pathology. No new reports appeared.

Laboratory Data. Four of eight patients with psoriatic arthritis had a negative agglutination reaction to hemolytic streptococci, and two of the four positive reactions were very faint.²¹²⁹ But in a group of 53 patients, the streptococcus agglutination re-

action was positive in 66 per cent.208

X-ray findings were regarded as indistinguishable from those of rheumatoid arthritis except for the unusual location. 1679 Joint changes of gout and syphilis may simulate psoriatic changes. If x-rays show early destructive change in the terminal joints with no significant loss of density, psoriasis should be suspected and clinical confirmation sought. The very destructive form of joint involvement is exceedingly rare. 628

Etiology. A common etiologic factor for skin and joint changes seemed the logical assumption to some authors.^{298, 312, 1165} Others felt that psoriatic arthritis should be interpreted as a manifestation of a combined abnormality of at least two genes, one accounting for the psoriasis, the other for the constitutional predisposition of the joints to various types of diseases.¹⁰⁵ Studies regarding the etiology of psoriasis stressed the importance of psychogenic factors.¹⁴⁵⁵ In 86 Army patients with psoriasis, emotional maladjustment was much more frequent than in controls, and was related to the onset and course of the disease in some patients.²¹⁹⁷

Treatment. While no systematic studies of the effect of ACTH and cortisone on psoriatic arthritis were reported, occasional patients with psoriasis and rheumatoid arthritis were included in several series. 175, 178, 854, 1348, 1897, 1969 In one patient treated with cortisone and later with ACTH, the arthritis disappeared

promptly and the psoriasis improved slowly during each course. 854

The articular response was similar to that in uncomplicated rheumatoid arthritis. There was also improvement in the psoriasis,¹⁷⁵ but the joint and skin lesions returned when the drug was discontinued.¹⁸⁹⁷ The arthritis was more responsive to these hormones than was the associated psoriasis.⁸⁵⁷ In one series the only patient with arthritis who failed to respond to cortisone had mild psoriasis; in other patients with psoriasis and rheumatoid arthritis, both the skin lesions and the arthritis responded favorably.¹³⁴⁸ [Subsequent experience indicates that in rheumatoid arthritis associated with psoriasis, the response to these hormones differs little if any from the response in uncomplicated rheumatoid arthritis. The control of the skin lesions is irregular, incomplete and often temporary. There is insufficient information on the effect of ACTH and cortisone on terminal interphalangeal joint involvement, which some consider the only true psoriatic arthropathy, to warrant any conclusions.—Ed.]

Gold therapy was considered to have the same value, dangers and limitations in psoriatic arthritis as in uncomplicated rheumatoid arthritis.²⁰⁸

REITER'S SYNDROME

Numerous reports on this syndrome appeared. The majority of cases consisted of the usual triad of conjunctivitis, urethritis and arthritis (and at times diarrhea). 111, 630, 560, 655, 785, 786, 970, 1068, 1322, 1530, 1575, 2002, 2229 Undoubtedly the most extensive work was that of Paronen, 1380 who observed 334 cases in Finland. Of these, only 233 cases had the basic triad of symptoms. There continued to be no agreement as to the clinical content required for diagnosis of this syndrome; some would broaden the diagnosis to include those patients with the incomplete syndrome. 900, 1436, 1530 While the incidence in the U. S. Navy and Marine Corps appears to be gradually increasing, this may reflect only an increased awareness

of the disease.²⁰⁰² The total number of cases observed to date cannot be accurately determined because many of the reported cases do not represent the classic clinical triad, and in others gonorrhea was not adequately excluded.³⁴⁴

Clinical Data. The clinical course was usually prolonged; the majority of patients recovered completely within two to six months. Recurrences were noted in 15 per cent of patients in one series. With few exceptions Reiter's syndrome affected young men, but its occurrence in women was reported. 1630, 2242, 2254 Urethritis was the most common presenting symptom, 344 but in many cases arthritis or conjunctivitis marked the onset of the disease. 444, 372 Less common findings included stomatitis, transient diarrhea, cutaneous lesions and ocular symptoms, each of which has ushered in the disease.

Articular Involvement. Joint symptoms frequently predominate and are very rarely absent. In the majority of cases the arthritis is polyarticular, with pain, swelling, increased heat and effusion. The joints of the lower extremities are more frequently affected than joints of the upper extremities, and large joints more often than small joints. Advanced articular deformities and ankylosis 1767, 2077 were observed. The joint manifestations may simulate those of rheumatoid arthritis, with sudden onset in symmetrical joints.

Genitourinary Involvement. This usually consists of a mucopurulent discharge, but may be an acute copious discharge with pyuria, hematuria and frequency of urination. In addition to urethritis, prostatitis, prostatic abscesses, cystitis and hydro-

nephrosis have been reported. 72, 141, 665, 1757

Ophthalmic Involvement. Conjunctivitis seems to be the most common ocular manifestation, but severe ocular involvement was reported in several patients. Language Cases of interstitial keratitis, 284 corneal ulceration and iridocyclitis also were described. Recovery from the eye involvement usually occurs without impairment of vision. Similarities between Reiter's syndrome and Behçet's and Johnson-Stevens diseases were pointed out. 1232, 1694

Changes in the Skin and Mucous Membranes. Superficial circinate lesions were observed on the glans penis in 26 of 53 cases. 909 Widespread skin lesions may occur which are identical with keratodermia blennorrhagica. 372, 397, 510, 1860, 2059, 2236

Etiology. Despite extensive bacteriologic investigations, a specific etiologic agent has not been identified. Lymphopathia venereum,³⁶¹ an unidentified virus,⁷⁸³ a filtrable agent pathogenic for mice,⁴⁶⁵ a Grahamella-like organism,²¹¹¹ and pleuropneumonia-like organisms ⁴³⁰ have all been suspected. Harkness ⁷⁸⁸ was able to cultivate pleuropneumonia-like organisms from only three of 30 cases; but in another study, pleuropneumonia-like organisms were obtained from the urine or synovial fluid in three of four patients with this syndrome.²¹²⁶

A possible relationship to bacillary dysentery was considered.^{874, 1209, 2215} In 176 cases of bacillary dysentery there were 14 cases of arthritis, of which seven showed the classic Reiter's triad; this syndrome was thought to represent "toxic manifestations of bacillary dysentery." ²²⁴² But of 1,120 cases of bacillary dysentery in another study, none had arthritis; in 10 cases of Reiter's syndrome there was no evidence that an active or latent Shigella infection was responsible. ¹⁸²⁹ Short ¹⁸²⁹ suggested that the dysentery can activate or provide a portal of entry for the etiologic agent of Reiter's syndrome, and that post-dysenteric arthritis may be due to a secondary invader rather than to Shigella. Three cases were reported ⁹⁷⁰ from the Bahamas, where bacillary dysentery is unknown. In India, where dysentery is very common, Reiter's disease is uncommon. ⁸⁸ Among the British troops in West Germany nine cases

were reported in a period of nine months; none of these were associated with dysentery. 1436 Of particular interest is the high incidence of antecedent dysentery (96.4 per cent) in an epidemic of 334 cases of Reiter's syndrome in Finland. 1530 [All but 33 cases were seen during and following a widespread epidemic of Flexner dysentery in 1944. It was estimated that 0.2 per cent of patients affected with dysentery developed Reiter's syndrome, most of them within three to four weeks after onset of the dysentery. It is evident that the author included postdysenteric inflammation of eyes, urethra or joints in both sexes, in the absence of the complete triad. Nevertheless, the detailed data indicate that the findings and the course in well over one-half of these cases were clinically indistinguishable from the classic entity. It seems likely that postdysenteric arthritis can be clinically indistinguishable from Reiter's syndrome; it does not follow that the dysentery organism is necessarily the etiologic agent.—Ed.]

Treatment. The value of treatment with sulfonamides, penicillin, 597, 1614, 1757, 2171 fever therapy, 908, 1246, 1322, 1436, 1580 arsenicals 72, 141, 665, 1092 and gold salts 111, 763, 2171 is equivocal, considering the variable response to these therapeutic agents and the usual tendency for spontaneous remissions to occur. Streptomycin has recently been tried, 450, 864, 1029, 2009, 2126, 2236 with more suggestion of benefit to the genitourinary than to the articular involvement. Improvement in four patients was not sufficient to warrant definite conclusions. 2126 Complete remission of all symptoms followed a three-day course of aureomycin. 1126

The use of ACTH in three patients with Reiter's syndrome, and cortisone in one patient, was reported. The response in each instance was prompt and dramatic. However, withdrawal of the hormones was followed by a relapse of symptoms.

[Among recently reported cases are included those without some features of the "classical triad," and others that present one or more clinical manifestations in addition to those usually accepted as characterizing this syndrome. The suggestions that the terms infectious urarthritis 900 or idiopathic blennorrheal arthritis 1757 be substituted for Reiter's syndrome seem unwarranted. Until more is known of the etiology of this condition, little would be gained from broadening the "clinical triad" heretofore accepted as characterizing this syndrome.—Ed.]

NEUROPATHIC ARTHROPATHY: CHARCOT'S JOINTS

It has not been established whether these joint changes accompanying lesions of the central nervous system are secondary to trophic impulses, as Charcot postulated, or merely the result of repeated microtraumata to an insensitive joint (Volkmann, Virchow). The experimental work of Eloesser in 1917, although not conclusive, lent support to the "repeated microtraumata theory." ⁴¹⁴ While recent authors called attention to diminution or absence of afferent proprioceptive impulses which normally inhibit hypermobility of joints, and to hypotonia of muscles and of blood vessels as additional factors in pathogenesis, they generally accepted the major rôle of trauma on anesthetic joints. ^{414, 579, 1930}

Clinical Data. Lesions of the nervous system other than tabes dorsalis that may result in the so-called Charcot type of arthropathy include syringomyelia, trauma to spinal cord, trauma to posterior roots, cord tumors, congenital malformations (as spina bifida), spinal caries from tuberculosis, malignant tumors or other destructive processes, acute myelitis, poliomyelitis, leprosy, toxic neuritis and hemiplegic states.

Charcot-like joint lesions of the ankle or foot have also been described in diabetic neuritis.^{71, 579, 1483} Seventeen cases occurred in a series of 20,000 cases of diabetes, an incidence of one in 1,100.⁷¹ All cases occurred in long-existing diabetes (10 years or more), and there was definite evidence of neuritis, usually

severe, in 17 of the 20 cases reported. The earliest gross change detected was unilateral or bilateral thickening in the tarsal region. No fluid was present in the joint and the swelling was painless, without redness of the skin, heat or other sign of inflammation. The change progressed slowly and usually resulted in a thickened and flattened foot with tendency to eversion and external rotation. X-ray findings were similar to those in other neuroarthropathies, and in the one case that was examined, pathologic changes were similar to those found in Charcot's arthropathy secondary to lues.

The possibility of a Charcot-like joint developing in yaws was raised by a single case reported in a native of the Marshall Islands.¹⁸⁶⁶ [This patient had symmetrical joint disease involving the metacarpal phalangeal joints, knees and ankles, without neurologic lesions. The possibility that this was rheumatoid arthritis with secondary degenerative arthritis does not seem to be excluded.—Ed.] Painless neuropathy with x-ray findings resembling those in Charcot's joints was observed in a patient with pernicious anemia and severe subacute combined degeneration of the spinal cord. When x-rays of the hips and knees were obtained in 52 patients with pernicious anemia, degenerative joint disease was mild and infrequent in those without spinal cord changes. The most severe and excessive joint changes were seen in five of seven patients with severe neurologic abnormalities, in whom the lesions were "clinically and radiologically of the type of neuropathic arthropathies." ⁷⁵⁸ One patient presented bilateral neuropathic elbows associated with bilateral cervical ribs and bilateral neuritis. ¹⁰⁰⁰ Multiple symmetrical joint involvement was reported in a tabetic patient. ⁶⁷³

The bone changes and soft tissue ossification in the pelvis and lower extremities of soldiers with spinal cord injuries (usually transverse myelitis) from war wounds and accidents were described in detail.^{838, 1887} Osteoporosis was followed by erosive bone changes leading to loss of normal contour of the trochanters, followed by reshaping and later repair with proliferative or exuberant bone and extensive soft tissue calcification. The process was considered comparable to the "hypertrophic" type of Char-

cot's joint.

Pathology. The primary pathologic change is a degeneration and partial disappearance of the joint cartilage, which is invaded by a fibrous tissue from the pannus on its surface. In certain areas the zone of preliminary calcification is exposed by the stripping away of cartilage. Beneath this zone there may be a proliferation of cartilage which becomes converted into subchondral bone, thus accounting for the sclerotic, eburnated bone seen at the base of large defects in the articular cartilage. A generalized atrophy of the trabeculae of the cancellous bone is often seen. [This is probably the basis for the pathologic fractures so commonly seen about tabetic joints.—Ed.] Intra-articular and extra-articular osteophytes, exostoses, ossification of muscles and ligaments, as well as ossification of joint cartilage, often occur.⁴¹⁴

An important finding helpful in early diagnosis of neuropathic joints was described.⁸³¹ Bits of bone and cartilage debris ground into the synovium and associated tissue were found in all of 24 neuropathic joints examined. In five patients, surgery was done for "osteoarthritis," but tabes dorsalis and Charcot's joints subsequently became obvious. The finding is not pathognomonic; it was observed in two of 12 cases of severe degenerative arthritis, but not in other

conditions.

X-Ray Findings. Møller 1415 described the roentgen findings in tabetic joints: "They present a multivarious picture, characterized on the one hand by

very considerable destruction of the ends of the joints; on the other hand by enormous, luxuriant new bone formations, which may completely surround the joint like spongy mass. Besides, numerous free joint-mice are formed, and large pegshaped bony outgrowths, so that the joint and its surroundings may assume quite fantastic shapes. These changes may develop rapidly or slowly. They may be found roentgenologically when neither patient nor doctor is aware of the presence of tabes dorsalis." He also stressed the frequency of spontaneous fractures about tabetic joints, and the very slight trauma that may produce them.

Treatment. No additions to the present unsatisfactory treatment were suggested. Attempted surgical fusion failed in 10 of 12 Charcot's knees, and in all of three Charcot's hips, *** but special methods for obtaining rigid fixation at

operation were successful in the knees.1478

EPIDEMIC TROPICAL ACUTE POLYARTHRITIS

This "new form" of epidemic rheumatism was observed in Australian and American troops stationed in Northern Territory and Queensland, Australia, and in Bougainville in the Solomons during certain seasons from 1942 through 1945. Its chief features were acute polyarthritis, mild fever, transient rash and lymphadenopathy. It was considered probably endemic in the Northern Territory of Australia, but its occurrence had gone unnoticed because the peacetime population was small. The features of more than 371 cases noted in seven reports between 1943 and 1945 have been reviewed (Ninth Rheumatism Review). In three subsequent publications the characteristics of the syndrome were confirmed.

Of 94 patients who contracted the disease in North Queensland during the wet season, all had mild fever and pain and stiffness in the joints, but only three had joint effusions. Rash was present in 90 per cent, lymphadenopathy in 50 per cent. Limited studies for bacteria and viruses were negative; circumstances again suggested an insect vector, possibly a mosquito. The term "epidemic acute polyarthritis" was thought to suggest a more severe disease than the clinical picture warranted, and "epidemic polyarthritis" was preferred. In a second epidemic occurring 15 months after one previously reported in the same area, 51 soldiers were affected within one month. The disease was mild; only 16 patients required hospitalization. Swelling of the joints was observed in 15, but in only two was there definite effusion. Dysentery or other enteric infection did not appear to be a probable cause. A biting fly was suspected as a possible vector.

Crain and summarized the features observed in the various epidemics. He distinguished the condition from dengue, acute rheumatic fever, early rheumatoid arthritis, palindromic rheumatism and Haverhill fever.

[Apparently the last reported observations on this disease were made in 1945. Of interest is the reference to a pre-war report of a syndrome with many similar features—J. R. Nimmo, 1928, cited by Gosling.—Ed.]

HEMOPHILIC ARTHRITIS

Hemarthrosis was considered perhaps the most common manifestation of hemophilia. Elbows, knees and ankles were most commonly affected, with sudden onset of swelling, warmth and pain lasting for a week or more. Frequent recurrences were the rule, and it was unusual for affected joints to return completely to normal. Careful protection and splinting of the acutely afflicted joint were recommended. [Early aspiration of the joints after use of transfusions will minimize permanent joint damage.—Ed.] Caution in the use of physical therapy during the recovery stage was advised. "It is a mistake to be in too much of a

hurry to move these hemarthrotic joints." 2167

Cystlike changes in the left iliac bone and calcifications about both hip joints were reported in a patient with hemophilia. In reviewing the bone and joint changes in 44 cases of hemophilia, Ghormley 637 found tumors (hemophilic pseudotumor) in the shafts of bones in six cases, and suggested that they arise either from hemorrhages into the joint extending along the bone or from periosteal hemorrhages.

RHEUMATIC PURPURA

Henoch-Schoenlein purpura is characterized by the combination of purpura or urticaria, arthritis or arthralgia, and abdominal pain. The arthritis was described as cyclic and as clearing without residual; in this respect it resembles rheumatic fever. In rheumatic fever the joints are usually red and hot, but not in rheumatic purpura. Also considered in differential diagnosis were serum sickness, drug allergies, meningococcemia and rickettsial diseases, and disseminated vascular diseases. In one fatal case, "when the knee joints were opened, the articular cartilage was well preserved, and when synovial tissue was examined microscopically, no inflammation was observed." 318

One fulminating case, which ended in death chiefly because of renal involvement, showed hemolytic streptococcus A in the throat prior to death. This, coupled with a history of previous rheumatic fever, led the author to suggest the presence of a "hypersensitivity angiitis." ²⁶ ACTH therapy brought about rather

prompt remission of symptoms and signs in a child. 1988

PALINDROMIC RHEUMATISM

This uncommon clinical entity, described by Hench and Rosenberg in 1941, continued to arouse considerable interest and controversy. Sixteen new cases were reported under this title during the period covered by this review, but of these only seven adhered strictly to the criteria used in the original description. 180, 045, 022, 1403, 2203 The clinical characteristics were summarized as multiple afebrile attacks of acute arthritis with pain, swelling, tenderness, varying degrees of redness and increased heat, and frequent recurrences lasting a few hours to a few days. Usually only a single joint was involved, with considerable disability at the time of attack but with complete restitution of joint appearance and function following attacks. Para-articular involvement and intracutaneous or subcutaneous nodules occurred in some cases. The absence of general constitutional signs and symptoms, the absence of chronic arthritis even when the disease had persisted for years, and the finding of essentially normal sedimentation rates, blood uric acid and radiographs of the involved joints were important points in differentiation. 180

Salomon 1768 reported four cases in children under 11 years of age in whom paraarticular involvement was prominent. Fever was associated with onset in two. "The proper inclusion of these cases is doubtful inasmuch as all attacks subsided perma-

nently within a few weeks." 2208 Perl's case 1888 was observed during almost two years; remission in joint symptoms occurred with bed-rest, and recurrences were associated with activity. Scheinberg 1778 reported a 43 year old man with congenital heart disease who experienced very painful involvement of large joints, with redness and swelling, recurrently over a seven year period. [Gout was not ruled out in this report.—Ed.] Gryboski 780 thought that joint pain and tenderness associated with recurrent nodular eruption in a woman with glandular tuberculosis were typical of palindromic rheumatism. Low grade fever and elevated sedimentation rate were attributed to the tuberculosis. [Some would consider this an excellent example of Poncet's disease.-Ed.] Weber 2186 felt that the term should be extended to include intermittent or recurrent hydrarthrosis, angioneural arthrosis and allergic rheumatism, and that the etiology was probably allergic. He described two cases briefly. The first patient suffered from recurrent hip pain, migraine and iritis, but did not have objective joint findings, and the disease showed no real similarity to palindromic rheumatism as defined by the originators of the term. The second case, regarded as "half way between palindromic rheumatism and angioneurotic edema" later showed radiologic changes and microscopically characteristic rheumatoid nodules.261 [In their original descriptions. Hench and Rosenberg carefully differentiated palindromic rheumatism from intermittent hydrarthrosis, "angioneural arthrosis" of Solis Cohn (1913) and the "allergic rheumatisms" of Kahlmeter (1939). While these conditions etymologically can be termed "palindromic" in the sense of "recurring" or "subsiding without coming to a head," their inclusion in the concept of a well distinguished clinical entity could serve only to compound confusion .- Ed.]

Additional Data. The clinical information from the original descriptions of 34 cases and nine detailed cases reported prior to 1946 was summarized in the Ninth Rheumatism Review. Of the seven characteristic cases reported in the next five years, four were in men, three in women. Ages ranged from 31 to 53 years. The disease had lasted from 21 months to 13 years without producing clinical or roentgenographic evidence of residual arthritis. Attacks lasted a few hours to a few days; usually only one joint was affected, but at times several were involved. Para-arthritis was noted at times in six, nodules in one. Slight elevation in sedimentation rate was present in three; one had an eosinophilia of 15 per cent during attacks. You biopsies were made.

No new information regarding pathology, etiology or prognosis was added. One patient experienced remission during trips to Florida ⁶⁴⁵; in two cases local trauma appeared to be a factor in some attacks. ^{922, 2203} Emotional tension and

anxiety seemed important in one 1463 but not in three others. 180

Treatment. Chrysotherapy was used in four patients, all of whom experienced a striking decrease in frequency of attacks amounting to a virtual remission. Ginsburg 445 initiated treatment with gold thioglucose in one patient 13 years after onset. He had been observed for six years, during which time the pattern of his disease had not been influenced by 29 different therapeutic measures. Some improvement was noted in six weeks, when total dosage of gold was 100 mg. After four months the patient had received a total dose of 440 mg. and had been symptom-free for two months. In three well documented cases, Boland and Headley 180 observed improvement when cumulative dosage of gold thioglucose totaled from 375 to 625 mg., and virtual remission after total dosage of 575 to 1,175 mg. On maintenance dosage at three-week intervals, remissions had lasted 18, 16 and six months. Frequency of attacks was reduced from an average of 73 per year to one in 18 months in one patient, from an average of 228

per year to four per year in a second, and from an average of 83 per year to none in six months in a third.

Benadryl was ineffective in three patients. 180, 645

Palindromic Rheumatism vs. Episodic Rheumatoid Arthritis. Hench 847 reiterated his position that in most cases palindromic rheumatism can be readily differentiated from atypical rheumatoid arthritis, in which there are periodic bouts of transient arthritis for months or years before it settles down to progressive joint involvement. He pointed out that in "episodic rheumatoid arthritis" the attacks tend to occur in favored joints and to last longer, that they may run together, that paraarthritis is rare or absent and finger-pad involvement does not occur, that constitutional manifestations and sedimentation rate elevation are more likely to be found, and that residual symptoms persist between attacks which are likely to be overlooked by both patient and physician. Boland and Headley 180 indicated the practical difficulty in differentiation in some cases; two patients presented some features of each condition, and a third developed progressive joint changes after a 13-month course typical of palindromic rheumatism.

A detailed and thoroughly documented instance of recurrent transient joint involvement in which radiologic changes were delayed for nine years was reported by Bywaters.²⁰¹ In addition to recurrent involvement of and around joints characteristic of palindromic rheumatism, the coarse was featured by recurrent intracutaneous nodules of digital pads, by acute swellings in tendon sheaths and palmar fascia producing transient finger contractions, and by bursitis. Biopsy of nodules and joints yielded findings regarded as diagnostic of rheumatoid arthritis. The condition was regarded as a variant of rheumatoid arthritis, and four additional cases were cited to illustrate

the transition to the more usual type of rheumatoid arthritis.

To Boland and Headley the beneficial results from gold therapy did not necessarily indicate that palindromic rheumatism represents merely an atypical form of rheumatoid arthritis, but if further trials substantiate their experience some weight may be added to that contention. ¹⁸⁰ Others stated that "it would indeed be difficult to regard a condition in which joints may survive hundreds of attacks without residual damage as identical with a disease in which a large number of attacks invariably leads to permanent and manifest injury." ²²⁰³

[We are in agreement with Hench's position that, until such time as knowledge of the cause of one or both conditions permits determination of the relationship of palindromic rheumatism to rheumatoid arthritis, it is worth while to study and differentiate this clinical syndrome descriptively. Nevertheless, the tendency to use this diagnosis to express wishful thinking on the part of physician and patient is to be deplored. Some of us have yet to see a patient in whom this diagnosis has been entertained who has not subsequently developed definite rheumatoid arthritis. To be of any value, the differentiation must adhere to the definite criteria stated by Hench and Rosenberg, particularly the requirement of several years of observation without residual joint damage. The experience of several of us suggests that palindromic rheumatism is much less common than an episodic onset of rheumatoid arthritis.—Ed.]

"ALLERGIC ARTHRITIS"

A factor of allergy is suspected by some to be concerned with the production of several types of joint disease, as noted in appropriate sections of this review. Serum sickness and related reactions to drugs are discussed under "Pharmaceutic Arthritis and Arthralgia." This section is concerned with "allergic arthritis" in the narrower sense of an articular reaction repeatedly provoked by a specific antigen, and relieved by permanent removal of the antigen.

These criteria were reasonably well met by four cases reported "to call attention again to the possibility that intermittent swelling of various joints in the body may occasionally be of allergic origin." 373 One patient had severe pain in neck and right arm, with swelling of right shoulder and upper arm, as well as finger involvement, of five months' duration. Clinical sensitivity to specific foods was demonstrated; their elimination was followed by complete relief. This patient had previously experienced a drug reaction with joint swelling and urticaria. A 40 year old man had recurrent attacks of joint inflammation and urticaria which could be reproduced by ingestion of peanuts and almonds. Reagins to these were demonstrated by passive transfer; when these foods were withdrawn, no further attacks occurred. In another patient with typical angioneurotic edema due to egg sensitivity, ankle and wrist swelling was at times associated with the edema. In a fourth, attacks of pain and swelling in the fingers lasting a few hours to a few days were provoked by ingestion of fish, and the attacks ceased following its elimination. The mechanism of production of joint symptoms was suggested to be probably the same as that underlying angioneurotic edema.

[It is important in such studies that the offending foods be identified by clinical trial. Most allergists consider skin tests of little or no value in the diagnosis of food allergy.—Ed.]

Somewhat less convincing were three cases of recurrent hydrarthrosis reported under the title of "allergic arthritis." 1403 In one patient with periodic attacks there was evidence of unrelated skin and nasal allergy, and skin tests to numerous foods were positive. Improvement was noted when the patient was placed on an exclusion diet and also given antihistaminics. The second patient had recurrent effusions of the knees in association with arthritis in other joints. The only evidence of allergy was a biopsy compatible with periarteritis nodosa; elimination of foods which gave positive skin reactions had not improved the arthritis. In another patient with cyclic intermittent hydrarthrosis, the only evidence of allergy was an eosinophilia of 8 to 12 per cent; allergic studies were negative, and the patient was placed on an exclusion diet without relief.

INTERMITTENT HYDRARTHROSIS

This condition was said again to occur in two forms: (a) symptomatic, in which recurrences are irregular, the duration of attacks increases, the joint does not return entirely to normal between attacks, and the condition eventually progresses to clear-cut rheumatoid arthritis; and (b) idiopathic, in which there is regular periodicity and the condition does not progress to eventual rheumatoid arthritis. An example of intermittent hydrarthrosis of four years' duration was included in a group of patients having various types of "periodic disease." 1661 Three cases of recurrent hydrarthrosis, of which two were periodic in recurrence, were reported as examples of "allergic arthritis." 1403 [The term intermittent hydrarthrosis should be reserved for those uncommon cases in which periodicity is regular, complete restoration of the joint to normal is observed between episodes, and no evidence of progression to residual damage is evident over a period of several years. Even when these criteria are adhered to, some of these "idiopathic" cases eventually turn out to be rheumatoid arthritis (Ninth Rheumatism Review). Some of us believe the condition to be an atypical form of rheumatoid arthritis.—Ed.]

PHARMACEUTIC ARTHRITIS AND ARTHRALGIA

Most joint manifestations related to the use of drugs or other therapeutic agents appear to be related to sensitization; some of them furnish the most convincing examples recorded of "allergic arthritis."

An apparent exception was the development of painful osteoporosis in about 2 per cent of patients receiving potassium thiocyanate treatment for hypertensive disease. Symptoms began insidiously three to six months after the drug had been started. Pain, usually in the lower extremities, gradually became more severe and was followed by mild swelling of the joints, without acute inflammation. Relief was not obtained by various measures as long as the thiocyanate was continued, but did ensue in all of 11 patients when the drug was stopped.*

Articular Reactions to Penicillin. Articular manifestations due to sensitivity to penicillin have been widely recognized, nearly always as a part of a serum sickness type of reaction. The most common pattern was a delayed type of reaction occurring a few days to a few weeks after penicillin administration. Features were malaise, mild fever, tachycardia, urticaria (usually severe and spreading), at times lymphadenitis, and often angioneurotic edema. Joint involvement ranged from arthralgia, usually severe, to localized joint swelling and at times effusions. Some reactions occurred within a few hours to two days after the first use of penicillin, 628,1131, 1729 and both early and delayed type of reaction occurred in one patient. The While these usually followed intramuscular penicillin, systemic reactions including joint manifestations were reported following oral penicillin, 831, 1780

Nearly all the features and variants of classic serum sickness were described in certain patients, including toxic psychoses^{1116, 1976}; abdominal symptoms, dyspnea and wheezing ¹³⁰⁶; and Schoenlein-Henoch purpura. The clinical and laboratory findings may lead to confusion with rheumatic fever. In one case electrocardiographic abnormalities of the ventricular complex were noted. The same services are described in complex were noted.

penicillin have been reported.188

In a review of reactions to penicillin, "based on 308 (of nobody knows how many more!) papers published on this topic from March 1943 to October 1948, and an additional 52 papers in which sensitivity is mentioned but neither defined nor described," Brown ²²⁶ collected the divergent views as to the mechanism of penicillin sensitization. There was no agreement as to importance of previous use of penicillin, previous history of allergy, the value of skin tests or the rôle of previous or concomitant fungus infections. Clinical and experimental studies demonstrated that crossed sensitization to crystalline penicillin and fungus products could be produced. ³⁸⁴

Articular Reactions to Sulfonamides. Arthralgia, usually in association with skin reactions and sometimes with other evidences of serum sickness, was included in

a review of reactions to the sulfonamides. 658

Serum Sickness. No new clinical data appeared. From further studies on the mechanism of serum sickness, it was concluded that this condition is the result of an antigen-antibody reaction, and that the serum sickness antibody is distinct from precipitin antibodies.^{1036a}

Treatment. State and Wangensteen 1920 encountered serum sickness after intravenous administration of crystalline bovine albumin, during investigation of this material as a blood substitute. When they undertook the use of intravenous infusions of procaine to relieve the arthralgia and myalgia, the entire clinical pic-

ture of serum sickness was favorably influenced. Following 1 gm. of procaine given over a period of two hours, 10 of 16 patients were completely relieved and four were temporarily relieved; only two were not helped. Another patient with serum-sickness reaction from tetanus antitoxin was similarly treated, with good results. Intravenous procaine was used in the treatment of penicillin reactions, with and without favorable results.^{226, 331, 1720} Antihistaminics were useful in controlling the skin lesions in serum sickness.¹⁵⁶³ [No mention is made of effect on arthralgia or myalgia.—Ed.] The somewhat inconsistent effects of antihistaminics in controlling penicillin reactions were reviewed: "they may or may not control the reactions and permit continuation of penicillin therapy." ²²⁶ [Cortisone and corticotropin have since been shown to control effectively both the urticaria and arthritis.—Ed.]

ALKAPTONURIA, OCHRONOSIS AND OCHRONOTIC ARTHRITIS

Alkaptonuria designates a condition in which certain aromatic compounds are excreted in the urine; these compounds (alkapton bodies) are characterized by the production of a dark or black color on oxidation, and by numerous chemical reactions. Ochronosis designates the pigmentation of tissues, particularly cartilage, which appears black grossly but derives its name from its yellowish appearance under the microscope. It is usually associated with severe or long standing alkaptonuria. With time, the ochronotic pigmentation may be associated with extensive cartilage degeneration, resulting in a distinctive form of arthritis. Especially characteristic are the spinal lesions that are secondary to intervertebral disc degeneration (Ninth Rheumatism Review). Pathogenesis 493 and historical aspects 348 were reviewed.

Clinical Data. Twenty-eight new cases of alkaptonuria were reported, including 14 with arthritis and eight with ochronosis. An ochronosis-like pigmentation of skin, nail beds, palate, conjunctiva and cartilage was observed in 10 men who had taken atabrine for from one to two and one-half years. None had alkaptonuria or x-ray evidence of arthritis. 1984

Spinal manifestations predominated in the five cases described in detail.^{243, 374, 493, 1995, 2161} In a 29 year old soldier, recurrent intervertebral disc herniation was associated with alkaptonuria and ochronosis; the symptoms dated from an injury at the age of 19.⁴⁰³ In the other four patients osteoarthritis of the spine was severe. In addition, one had loose bodies and degenerative changes in the knee, ¹⁹⁹⁸ and two had involvement of other peripheral joints.^{343, 2161} The problem of diagnosis was well illustrated in the instance of a 35 year old man with low back pain that had resisted a variety of treatments. The extensive disintegration of intervertebral discs, with apparent displacement of vertebrae in the settling process and lipping of all lumbar bodies, was unexplained until homogentisic acid was demonstrated in the urine and ochronosis of ear cartilage was demonstrated by biopsy.³⁷⁴ Calcification of intervertebral discs was again noted.²¹⁶¹

Alkaptonuria appeared as a simple recessive characteristic in a study of a large American family. Fifteen cases were found among 300 relatives investigated from a large kindred, traced through seven generations. Arthritis and ochronosis were associated with the alkaptonuria in three cases, and arthritis alone in two.⁷³⁸ The importance of intermarriage was indicated by the family history of a patient with alkaptonuria, ochronosis and arthritis. His parents were first cousins, three of his eight siblings had alkaptonuria, and two of the three had arthritis also. The patient had

married a cousin, and three of their four children had alkaptonuria, two having arthritis also.2161

Laboratory Data. Chemical tests used in detecting alkaptonuria were listed.^{843, 493} A new observation of fluorescent behavior of urine containing alkaptone bodies was made.³⁴³ Another instance of alkaptonuria and hyperuricemia was recorded.²¹⁶¹ ["Blood" uric acid was 6.8 mg. per cent, method of determination not stated. There were no clinical characteristics of gout. It is likely that alkaptone bodies may contribute to the color produced with several of the reagents used for determination of uric acid.—Ed.] Neuberger ¹⁴⁶⁶ criticized the specificity of older methods for determination of homogentisic acid and described a specific quantitative silver-reduction method.

Pathology. In a 59 year old man who had died of myocardial infarction, autopsy revealed severe atherosclerosis with pigmentation of the intimal surfaces of aorta and large arteries, accentuated at the sites of arteriosclerotic plaques. In addition to pigmentation of skin, conjunctivae and all the cartilages, shades of bluish black were found in fascial planes, tendons, ligaments, perichondrium, periosteum and other connective tissue structures. Bluish black fluid was found in the larger joint spaces. Secondary to the cartilage pigmentation, a crumbling, fragmenting degenerative process had resulted in destruction of the articular surfaces, intervertebral discs, symphysis pubis, and sterno-manubrial articulation. The intervertebral discs had collapsed in varying degrees, with osseous union between several of the vertebral bodies.

Etiology and Pathogenesis. Alkaptonuria was again designated as a congenital defect in metabolism of the amino acids tyrosine and phenylalanine. Presumably because of the lack of an enzyme required to open the benzene ring, in these individuals the breakdown of the above precursors is blocked at the stage of homogentisic acid. rather than going on to yield acetone, as in normal persons. When tyrosine or phenylalanine was administered to alkaptonuric subjects, 85 per cent of the dose was recovered as urinary homogentisic acid in one patient 1467 and 52 per cent in another.2161 No significant effect on homogentisic acid excretion was noted following ingestion of ascorbic acid, cysteine or methionine.1467 Failure to alter the rate of excretion by thiouracil and para-aminobenzoic acid suggested that the enzymes involved in converting tyrosine to homogentisic acid were not the same as the tyrosinase involved in conversion of tyrosine to melanin.2161 The very low plasma concentrations noted in a six year old subject, even after the feeding of aromatic precursors, led Neuberger 1467 to emphasize the rôle of the kidney in either the formation or the active tubular excretion of homogentisic acid. [Further observations on plasma levels of alkaptone bodies are needed. The results of this study are counter to the accepted theory that ochronosis results from high levels of pigmenting material in the circulating blood.—Ed.] Experimental alkaptonuria was induced in rats by dietary deficiencies of various amino acids. 1408

Treatment. No effective methods of treatment were suggested.

[In addition to its clinical recognition, this condition is of interest to students of rheumatic disease on theoretic grounds. It provides an excellent example of a metabolic product which hastens cartilage degeneration and accelerates the development of degenerative joint disease. Has this been recognized only because the product involved happens to be pigmented, and may there be nonpigmented products with comparable effects on cartilage?—Ed.]

"METABOLIC ARTHRITIS"

Gout and ochronotic arthritis can be regarded as examples of "metabolic arthritis." There are no other clearly defined entities which come under this heading. The relationship of "metabolic dysfunction" to various types of arthritis

was speculated upon.¹²⁷⁶ In a study of the oxalic acid content in the blood of patients with "more or less marked metabolic disturbances," four patients with severe joint pains "caused by faulty oxalic acid metabolism" were mentioned.⁷²⁷ [No clinical data were given.—Ed.]

ENDOCRINE ARTHRITIS

With the possible exception of acromegaly, no specific endocrine disorder has been identified with a particular type of joint disease. The evidence for and against the implication of hormonal dysfunction in the pathogenesis of various forms of arthritis is reviewed in appropriate sections of this Review, especially in "The Adrenal Cortex and Rheumatic Diseases."

Menopausal Arthritis. It was stated, without new evidence, that hormonal dysfunction may be responsible for the onset or exacerbation of many of the arthritides occurring at or after the menopause. The controversy surrounding menopausal arthritis seemed to be concerned with the pathologic classification of the arthritic condition, rather than with the recognition of painful joints as an entity in the complex syndrome of the climacteric. "Patients with arthralgia associated with the change of life may show no demonstrable pathologic change in the joints. In those who do show changes, atrophic arthritis is more common than the hypertrophic variety." The use of general supportive measures was emphasized, in addition to large doses of estrogens, and adjunctive thyroid therapy in some instances. "The status of endocrinotherapy in the arthritis occurring at or after the menopause is not as yet defined." 210 [With this statement we can agree.—Ed.]

THE PAINFUL SHOULDER

Although cases of painful shoulders are apparently becoming so numerous that they are now "encountered almost daily by the general clinicians," 1506 the confusion pointed out in previous Reviews continues to surround the subject. Uniform terminology still has not been established. Thus, although most persons who have explored the shoulder agree with Codman's classic descriptions (1934), and maintain that calcific deposits rarely are located primarily in the bursa, the popular terms "subacromial bursitis" and "subdeltoid bursitis" persist. 23, 89, 1343, 1384, 1306, 1540, 2037, 2237, 2238 "Peritendinitis calcarea," "bicipital syndromes," "periarthritis," "peritendinitis," "Duplay's disease," "frozen shoulders," "internal derangement of the subacromial mechanism," "the supraspinatus syndrome," "adhesive capsulitis" and "irritative capsulitis" were terms used to describe conditions giving rise to pain in the shoulders. 22, 138, 474, 774, 1108, 1352, 1356, 2032, 2196 Some physicians included the "shoulder-hand syndrome" as a manifestation of painful shoulder. 28, 403, 1382

Anatomy. The anatomy of the shoulder girdle was described by Nauta 1461 and by Quiring and Boroush, 1615 who also traced its evolutionary development, while the innervation was described by Wrete. 2223 The long head of the biceps brachiae was described in detail and its relationship to painful shoulders discussed. 802

Clinical Course. Young 228 has listed more than 30 conditions which will cause pain in the shoulder. Despite this multiplicity of etiologic factors, uncertainty of diagnosis and confusion in terminology, most cases of purely localized

painful shoulder apparently fall into one of several distinct clinical categories. The first of these is characterized by acute onset, severe pain in the shoulder and localized tenderness, usually over the region of the subacromial bursa. Although pain is present even at rest, it is markedly accentuated by motion beyond a few degrees, particularly by elevation of the arm and by internal rotation. X-ray may reveal a calcium deposit in the musculotendinous cuff, and usually but not always in the tendon of the supraspinatus overlying the subacromial bursa. After several days of severe pain the acute symptoms usually tend to subside but do not disappear entirely. In other cases the onset is less spectacular and abrupt; this is the condition popularly called "subacromial or subdeltoid bursitis." However, since it is comparable to calcific tendinitis elsewhere in the body, this term would seem appropriate also for the condition when it occurs in the shoulder. 1084, 1361, 1915

The exact relationship of a calcium deposit to pain in the shoulder is not clear. Some authors maintained that an acutely painful shoulder will be relieved when the deposit ruptures, either spontaneously or as the result of needling, into the subacromial bursa. 266, 1005, 1361 Others suggested that irritation of the bursa by the calcium produces the pain. 501, 1189, 1489, 1536, 1934 The etiology of calcific tendinitis in the shoulder is unknown. Degeneration of the tendon (which is probably related to "wear and tear") was thought to precede calcification. 511, 1084, 14714, 1489, 1034 It was reported to be more frequent in females than in males, 551 and to be rare in Negroes. 1691

Various forms of treatment were recommended. Although differing as to dosage, most writers felt that x-ray therapy, when administered early, is almost specific and brings prompt subsidence of symptoms. 3, 610, 896, 1177, 1188, 1249, 1353, 1480, 1691, 2232, 2237 Others favored needling and procaine injection. 290, 1361, 1489, 1684, 1915 Various physical therapeutic modalities were recommended. 266, 474, 787 Less popular treatments included oral ammonium chloride, 1331 a vegetarian diet, 1189 and procaine injection in combination with vaccine and "counter-irritation." 89 Although x-ray therapy was usually thought to be of little assistance in the chronic states, it was reported to have provided relief in some cases of many months' duration. 1108, 2237 Surgical removal of the calcific deposit was considered advisable in chronic cases refractory to other treatments. 187, 1084, 1351, 1536, 2237 Some considered it the treatment of choice in acute cases also. 1084, 1548 One author suggested surgical excision of the tip of the acromium in chronic cases. 1861 [Although some favorable results with ACTH and cortisone have been reported since the period covered by this review, their place in the treatment of acute and chronic shoulder disorders has not been clearly defined.—Ed.]

Quite distinct from the above is the painful shoulder of gradual onset, with diffuse pain, no localized tenderness, and progressive limitation of motion, now generally referred to as "adhesive capsulitis." 151, 787, 14718 X-ray examination shows no calcific deposit in the tendinous cuff unless the condition develops secondarily to unrelieved calcific tendinitis. A certain percentage of the cases progress to the condition called "frozen shoulder."

Adhesive capsulitis of moderate severity may respond to physical therapy alone, but when it has brought about a frozen shoulder it usually requires manipulation under general anesthesia. 52, 133, 151, 266, 306, 787, 881, 1084, 1384, 1762, 2195, 2196 Some authors, however, believed that even the frozen shoulder can be relieved by physical therapeutic measures alone. 121, 290, 474 Although the exact etiology of the frozen shoulder is a matter of conjecture, Simmonds 1846 believed it is due to chronic inflammatory reaction of the supraspinatus tendon secondary to degen-

erative changes which are probably associated with impaired blood supply. This in turn may be due to injury of the tendon by impact against the acromium process. Meyerding 1284 also stressed the importance of repeated attritional trauma.

[The above distinction between calcific tendinitis and adhesive capsulitis seems arbitrary to some of us. While it is useful in the separation of "typical cases," many patients present clinical features which fall in between; cases with an acute onset may progress to a frozen shoulder, calcification may be visualized in either condition, and x-ray therapy is occasionally helpful in cases of adhesive capsulitis which represent a late complication of calcific tendinitis. Or the entire range of clinical manifestations may reflect different degrees and intensity of the same unknown fundamental process.—Ed.]

Less common causes of pain in the shoulder include arthritis (both osteoarthritis and rheumatoid arthritis), sprains, fibrositis and ruptured tendons.^{23, 89, 2238} Ruptured tendons are especially important as a cause of painful shoulders, since their early recognition and prompt surgical correction are essential to save the patient continuing distress.⁷⁸⁷ The rôle of degeneration of the supraspinatus tendon as a precursor to rupture was demonstrated in a cadaver ²²¹⁶ and experimentally in rabbits. X-ray demonstration of cystic areas in the head of the humerus may indicate a degenerative process associated with tearing of the tendon.⁸⁰⁸

Pain in the shoulder may also be due to conditions outside the shoulder itself. The most important of these are the conditions giving rise to the reflex dystrophy of the upper extremity (the shoulder-hand syndrome) and brachial neuralgia, and are discussed under those headings.

REFLEX SYMPATHETIC DYSTROPHY

Synonyms and Related Conditions. Causalgia, Sudeck's atrophy (post-traumatic osteoporosis), painful disability of the shoulder following coronary occlusion, postinfarctional sclerodactylia, palmar and digital contractures, as well as Dupuytren's contracture, the swollen atrophic hand associated with cervical osteo-arthritis, and the shoulder-hand syndrome, probably all represent similar if not identical neurovascular mechanisms. 1946

The frequency of causalgic states following World War II wounds has revived interest in an entity whose earliest adequate description is generally attributed to Weir Mitchell during the Civil War. The subject was reviewed at some length in the last Review, and more recent papers tended to support the facts outlined there. 24, 276, 518, 519, 578, 788, 1327, 1402, 1555, 1600, 2058, 2081, 2135 Clinically. the condition first presents burning pain, nonsegmental in distribution but occurring in an extremity (usually, but not always, the site of recent trauma), followed shortly by nonpitting edema. As the edema spreads, the extremity shows cyanosis and becomes hard, brawny and less tender. Muscular atrophy and osteoporosis then become evident, increasing as the condition progresses, and the pain becomes "intractable." Hyperemia is usually considered the cause of the osteoporosis, but the vasomotor manifestations were found to be of two distinct types. vasodilatation and vasoconstriction, and in no case was there noticeable alteration in the type while the patient was under observation. Demineralization was present in both types but was more pronounced in vasodilatation. 1327, 1555, 2081 usual assumption that the condition tends to occur in psychoneurotic individuals was denied.2031

Pathogenesis. This is admittedly not clear, and theories presented are purely conjectural. According to the usually stated theory, first advanced by deNó in 1938,

a prolonged bombardment of pain impulses institutes a cycle of reflexes spreading through an "internuncial pool" of neuron connections upward, downward and across the spinal cord. This "internuncial pool" is considered to be a "closed self-reexciting chain" of synapses which, having once received sufficient stimuli to become activated. continues to send impulses into the sympathetic pathway until checked, either temporarily by procaine infiltration or permanently by sympathectomy, rhizotomy or cordotomy. However, Nathan 1460 concluded after an exhaustive review that the most satisfactory hypothesis was as follows: "stimulation of the somatic sensory axons occurs at the site of the lesion on the nerve trunk; this stimulation is caused by efferent impulses coming down the sympathetic outflow, the site of the lesion forms an artificial synapse where this stimulation occurs; the pains due to impulses arising at this synapse are referred by the patient to the area of distribution of the sensory nerve." [If this is somewhat confusing to the reader, let him not be discouraged, as the editors of this Review are not sure that even the writers on the subject have a clear notion of what it means. However, Steinbrocker's drawing 1946 illustrating deNo's theory is a most lucid attempt to clarify an admittedly obscure situation.-Ed.]

Treatment. Repeated procaine infiltrations of the sympathetic ganglia coupled with active physical therapeutic measures is the treatment of choice; however, sympathectomy may be necessary. Successful treatment with tetraethylammonium chloride was reported.^{276, 578} In cases which have persisted for some time, cordotomy, psy-

chotherapy or prefrontal lobotomy may be necessary. 276, 1402

The Shoulder-Hand Syndrome. This condition, only recently designated as a distinct clinical entity, was first summarized by Steinbrocker in a paper before the American Rheumatism Association, 1989 Subsequent papers by the same author and his associates 1944, 1945, 1946, 1947 have served to clarify the subject further and to identify it with the causalgia state. One of these 1946 summarizes in detail our present knowledge of the condition. Bayles 114 summarized 17 cases of this condition observed to follow various precipitating factors, but others writing on the subject 282, 805, 882, 1018, 1026 stressed the importance of the shoulder-hand syndrome as a complication of coronary artery disease. As pointed out in the last (Ninth) Rheumatism Review, the condition, although most frequently reported following myocardial infarction, may occur after hemiplegia, splinting of an arm after fracture, manipulation of a shoulder, in the convalescent period following an abdominal operation, or even without apparent cause. Usually unilateral, it may at times be bilateral. It occurs usually in patients in the older age Symptoms and signs follow a rather typical pattern and closely resemble those outlined above under causalgia. Either the shoulder or hand may be affected first, or the two may develop symptoms simultaneously. The shoulder presents generalized stiffness and moderate pain which becomes acute on attempted motion. The hand presents uniform generalized brawny thickening with tense, shiny bluish skin, the latter somewhat resembling a sclerodactylia. swelling is usually nonpitting, although in some acute cases a rather marked pitting may be present. The fingers are held in a position of partial flexion, with motion markedly restricted in the effort to avoid pain. The grip is weakened. Although the patient may complain of pain radiating from the shoulder to the tips of the fingers, the elbow remains singularly unaffected from an objective standpoint. These symptoms will usually become progressively worse during a period of from three to six months, following which the painful shoulder dysfunction gradually subsides, as does the swelling of the hand. At this stage, however, the stiffness and flexion deformity of the fingers are apt to become more

pronounced, with atrophy of the subcutaneous tissues and muscles of the hand. Dupuytren's contractures may ensue. X-rays reveal a diffuse osteoporosis.

Treatment of the shoulder-hand syndrome is the same as noted above for reflex dystrophy in general. It may be unsatisfactory, even when instituted early. Although active physical therapy must be carried out from the beginning, forced passive motion of either the hand or the shoulder may aggravate the condition. A single stellate ganglion block brought improvement in 10 of 16 cases. 992 A single case was reported that had been unsuccessfully treated with rather small doses of ACTH over a period of 11 days. 994 [There are later reports of the successful use of ACTH and cortisone, usually in somewhat larger doses than are used in rheumatoid arthritis.—Ed.]

BRACHIAL NEURALGIA

Radicular Pain in the Upper Extremity

Somewhat similar to the confusion surrounding the painful shoulder is the confusion regarding the various conditions which produce a radicular type of pain in the upper extremity. "In the differential diagnosis of pain in the neck and shoulder, experience may be fallacious and judgment difficult. The pain may be simply an annoyance or a symptom of serious disease. . . . These patients wander from physician to physician and often to cultists—and still the pain persists." ⁵³⁸ In reviewing the papers dealing with this chain of symptoms, it is obvious that various authors, although describing the same condition, are attributing it to different etiologic factors, while some seem unaware of the various conditions that produce somewhat similar symptoms. It would appear that our knowledge of these conditions is still incomplete and that a final answer is not on the immediate horizon. Several authors attempted to summarize and to classify the various conditions causing pain radiating from the neck and shoulder girdle into the upper extremities. ^{133, 153, 290, 420, 463, 538, 748, 900, 902, 999, 1465} Not all were in agreement, but the following entities should apparently be recognized:

Osteoarthritis. This was referred to both as a very common cause of nerve root involvement 902 and as an uncommon cause. 857, 838 The pain itself was claimed to be due to nerve root compression produced by bony spurs in the intervertebral foramina (this was called "facet syndrome" by one author). 153 and also to soft tissue or joint effusions rather than actual osteophyte formation. 902, 1817 Narrowing of the intervertebral disc spaces may result from degeneration, shrinkage and loss of elasticity of the intervertebral discs. 902 Chest symptoms simulating coronary artery disease may also arise from osteoarthritis of the cervical and dorsal spine. 308

Abnormalities of the Intervertebral Fibrocartilages. Hoffman 902 was of the opinion that degeneration of the cervical disc with bulging of the annulus fibrosus into the spinal canal should be regarded as a part of osteoarthritis and not of the disc syndrome. But midline protrusions of the disc sufficient to cause pressure on the cervical cord, or true ruptures with herniation of the nucleus pulposus, although rare, may present a picture likely to be confused with intraspinal neoplasms 537 or Pancoast's tumor. 1791 Posterolateral bulging of the disc without rupture, but still causing pressure on the cervical roots and not on the cord itself, was more frequently recognized as a cause of neck and shoulder pain. 153, 538, 600 These patients may present a variety of symptoms, chiefly stiffness of the neck, and pain over a period of months or years. The pain may be cervical, scapular, humeral, precordial or thoracic. It may be sub-

occipital or may radiate down the arm. Sudden changes of position of the head, coughing, sneezing or straining may aggravate the pain or may cause a sudden electric shocklike exacerbation of the pain. Paresthesia may develop, as well as muscular

atrophy.

Lesions of the Superior Thoracic Outlet. Several conditions were differentiated under this heading, all of which can be responsible for compression of the brachial plexus and subclavian vessels. In addition to the well recognized mechanisms of a cervical rib or abnormal scalene muscle in producing symptoms, a "costoclavicular syndrome" was described in which the neurovascular structures are compressed between the clavicle and the first thoracic rib. 1851, 1709, 1919, 2042 Any of these mechanisms may cause symptoms in three major systems: (a) Circulatory symptoms may be mild, giving only pallor of the extremity, or they may be severe enough to cause thromboses in the subclavian, radial or ulnar artery. (b) Nervous symptoms may be only mild paresthesia, or they may be severe continual pain and atrophy of muscles of the hand. (c) Sympathetic symptoms may involve vascular structures at the distal part of an extremity without affecting the proximal parts. 108

Recent writers have differed as to the significance of an abnormal scalenus anticus muscle. It was considered to be seldom a primary condition, but rather a common complication of any of the more prevalent afflictions of the shoulder girdle or cervical spine. 153, 413 Judovich 1017 suggested that a primary scalene syndrome is one in which symptoms originate in and are due to an intrinsic disturbance of the anterior scalene muscles (spasm, hypertrophy or myositis often due to trauma), while a secondary scalene syndrome is one in which there is reflex spasm of the anterior scalene muscle, caused by irritation of structures in the shoulder girdle or by disturbance of segments which innervate these structures. Recognition of this difference can explain the relief of symptoms which sometimes follows section of anterior scalene muscle (in primary cases), and its failure in others (when the syndrome is secondary to some condition outside of the muscle itself). He suggested that the two types may be differentiated by the relief of symptoms obtained in primary cases by proper injection of the anterior scalene muscle with novocain, but others questioned the value of this procedure in diagnosis. 1969 Similar symptoms may be due to an anomalous insertion of the scalenus medius muscle 1202 or to dropping of the shoulder girdle. 258 An excellent anatomic study of this area was presented. 1101

Treatment. Most of those writing on the subject of osteoarthritis of the cervical spine and of protruded cervical discs agreed that conservative treatment using diathermy, cervical traction and sometimes a neck collar should be given an adequate trial. If symptoms are not relieved, surgery is indicated. Cases of primary scalenus anticus syndrome may be completely relieved by section of the muscle. One cases of cervical rib syndrome may also be relieved by this procedure, whereas others will require removal of the rib. One of the costoclavicular syndrome, exercises to strengthen muscles which elevate the shoulder girdle were successful in about one-half of the patients; if the exercises failed, scaleniotomy and sometimes rib resection was advised.

NONARTICULAR RHEUMATISM

Nonarticular rheumatism embraces a variety of conditions in which musculoskeletal complaints are produced by conditions which do not involve the joints proper. The pathology of certain of these conditions is well defined in soft tissues such as bursae, tendons and tendon sheaths, muscles and fascia; in other conditions under this heading, the pathology responsible for the symptoms is hypothetic, or nonexistent, as in "fibrositis" and "psychogenic rheumatism." Many of the conditions considered in the sections on "The Painful Shoulder," "Reflex Sympathetic Dystrophy," "Brachial Neuralgia" and "Backache and Sciatica" can properly be classified as forms of nonarticular rheumatism. [Many of these conditions are poorly defined, and there is no apparent agreement as to classification. To add to the confusion, some authors use the term "fibrositis" as synonymous with nonarticular rheumatism, while others restrict its use to a loosely defined symptom-complex without characteristic localization or pathology, which is believed to constitute a clinical entity. In this review the editors have followed an arbitrary classification which seems logical to them, and have used "fibrositis" only in the second sense.—Ed.]

Diseases of Fibrous Structures

Bursae and Bursitis. All parts of the body in which movement is likely to produce friction are provided with bursae. Some are constant, others occasional; some superficial, others deep; some are constantly connected with joints, others never or only as an anomaly. Adventitious bursae arise at points of abnormal irritation, as in a bunion. When the subdeltoid bursa of rabbits was obliterated surgically, subsequent implantation of cellophane resulted in formation of a new bursa in 28 of 30 instances. Enlarged bursae are not all traumatic. Visualization by x-ray after an injection was suggested as a safe procedure to aid in the diagnosis of bursal enlargements, and to determine the anatomic connection of bursae with joints and the character of bursal contents.

Inflammation of a bursa (bursitis) may be caused by trauma, unusual use of the part, infection, or by some unknown agent.³³⁶ It was suggested that syphilitic bursitis may be more common than is usually suspected.²⁰⁴⁹ The pain of bursitis, particularly in the shoulder, was attributed to concomitant inflammation of the adjacent joint, and the term "acute calcifying burso-arthritis" was recommended.¹¹⁸⁹ [No pathologic evidence for this concept was submitted.—Ed.]

Locations of Bursitis. Commonly affected are the subacromial, olecranon, ischial, prepatellar and achilles bursae. Of these, subacromial bursitis is the most common, and the symptoms, signs, diagnosis and treatment were outlined in detail. It is further considered under "The Painful Shoulder."—Ed.] In the region of the elbow joint the olecranon bursa is vulnerable because of its superficial location. The resulting lesion, marked by localized tenderness and swelling, is often referred to as "miner's elbow." The other common disability about the elbow joint, "tennis elbow," is sometimes due to radiohumeral bursitis, 1913 but may be due to a lesion in other structures. [See Diseases Primarily Related to Trauma.—Ed.] Bursitis in the region of the fibular collateral ligament, confirmed in six patients by surgical removal, was responsible for pain over the lateral aspect of the knee, aggravated by exercise and relieved by rest. Examination revealed a localized tender mass at or near the ligament with pain on adduction of the tibia, extension of the knee, and internal rotation of the tibia on the femur. On the substantial rotation of the tibia on the femur.

Few cases of bursitis involving the hand have been reported, but among 523 injuries in boxers and wrestlers, traumatic bursitis of the metacarpophalangeal joints was diagnosed in ten. Seven responded to conservative treatment, but in three, excision of the bursal sac was necessary. Iliopectineal bursitis must be considered in the differential diagnosis of hip pain. Other symptoms are change in gait, flexion of the hip and knee, adduction and external rotation of the hip, and protection against hyperextension. Immobilization in a hip spica, with a window over the femoral

triangle to permit application of heat, was said to shorten the period of recovery.⁸²⁴
Fourteen cases of anserine bursitis (cystic hydroma of horsemen) and supernumerary bursa of the pectineus muscle simulating inguinal hernia ¹⁵⁵⁶ were described.

Calcareous bursitis in the region of the knee is rare but was found in eight patients who complained of progressive pain, swelling and limited movement. Examination revealed a tender swelling over the involved bursa. Calcification was usually not suspected until revealed by x-ray. A patient with calcification of the prepatellar bursa was also reported. and in one exceptional case the deposit invaded and penetrated the bony cortex. In another patient, calcareous deposit involved the radio-humeral ligament with extensive infiltration into the joint capsule, sufficient to suggest a neoplasm.

Treatment. Acute traumatic bursitis is best treated by aspiration of the fluid, gentle compression, rest, heat and physiotherapy. Some deep bursae may respond to procaine injections and deep x-ray therapy, but surgery is indicated in the persistent traumatic type with pathologic changes. 45, 1915, 2134 In calcareous bursitis, conservative treatment using needling and injection of procaine should be tried first if the symptoms are not too severe. If such treatment is unsuccessful, surgical excision may be curative. 63, 1484 Three patients were completely relieved when the bursae were injected with 3 to 5 c.c. of Intracaine in oil. 1201

may be due to specific infection, most often tuberculosis, 1960 or to acute or chronic trauma. It may occur in the course of rheumatoid arthritis, palindromic rheumatism, gout, or specific infectious arthritis, or it may develop without relation

Tenosynovitis and Tendinitis. Inflammation of tendons and tendon sheaths

to any of the above factors.

Nonspecific inflammatory lesions of tendons were divided into three groups: (1) peritendinitis crepitans, in which the deposition of fibrin produces characteristic crepitation on motion, and which is usually attributed to prolonged repetition of the same movement; (2) stenosing tenosynovitis, which occurs only in tendons whose synovial sheaths are constricted at the narrowest portions; and (3) tenosynovitis with effusion, most commonly due to tuberculosis, but not infrequently associated with rheumatoid arthritis. The frequency of tendon sheath involvement in rheumatic diseases was emphasized 1894; in rare cases it may be the primary lesion. In such a patient with nodular polytendovaginitis and no joint disturbance, histologic changes in the tendons were similar to those seen in rheumatoid arthritis. Subcutaneous nodules were present, and the patient had experienced relief during a bout of obstructive jaundice. 1895

Tenosynovitis in the forearm occurred in people whose work requires a strong gripping action while the hands are being subjected to vibration, for example, in workers catching bricks dropped from a height, or automobile mechanics using pliers. In three cases, tuberculosis of the tendon sheaths developed.¹⁶⁷¹ Tenosynovitis of the wrist and hand may produce considerable enlargement.¹⁹⁶⁰ Three cases of chronic nonspecific tenosynovitis, with effusion about the ankle, were reported.¹¹⁷²

The incidence of acute suppurative tenosynovitis of the hand has decreased to 42 per cent of what it was before the introduction of antibiotics.⁵⁶⁴ Penicillin was ef-

fective in all of 13 acute cases.378

Stenosing Tendovaginitis at Radial Styloid (Quervain's Disease). This condition is often a cause of persistent wrist pain. It results from hyperplasia and thickening of the sheath which envelops the tendons of the abductor pollicis longus and extensor pollicis brevis as they emerge from a common tunnel in the bony groove

over the radial styloid, beneath the dorsal carpal ligaments. In some cases a nodule or an inflammatory reaction in the tendon was recorded.^{78, 1594}

The onset is gradual, over a period of weeks or months. Trauma does not often appear in the case history, but excessive use of the hands may be a factor. The patient's chief complaint is pain on moving the thumb. Findings include (1) swelling over the sheath, obliterating the anatomic snuffbox; (2) localized, exquisite tenderness over the tip of the radial styloid; (3) thickening of the tendon sheaths on palpation; (4) pain on forcible abduction of the thumb; and (5) absence of heat, redness or crepitation. Roentgenograms are usually negative, but may show a periosteal reaction. Conservative treatment, including immobilization in plaster, local heat, x-ray therapy and physiotherapy, is seldom successful. Surgery is the treatment of choice; active movements should be commenced 24 hours after the operation. 486, 749, 786 In two unusual cases the constriction involved only the extensor pollicis brevis, which was in a separate compartment. 1463 The occurrence of Quervain's disease in a mother and daughter was reported. 2004

Other Tendon Lesions Around Hand. Unusual forms of tenosynovitis were described by several authors. Next in frequency to Quervain's disease as a cause of painful thumb movement was involvement of the flexor pollicis longus at the metacarpophalangeal joint. He Fourteen cases of "trigger-thumb" in infants were reported, in which the thumbs could not be fully flexed or extended; there was no history of injury or pain. The condition was due to fusiform swelling of the flexor pollicis tendon with constriction of the sheath at the metacarpal head. Surgery was successful in all cases. He causative factor. Two of the patients had been injured by handling an overheated arc-welding gun, and the third had received an overdose of infrared radiation. Sis cases of tenosynovitis of the extensor carpi ulnaris were described; this lesion had not previously been recorded. The usual cause was a twisting injury to the wrist. Examination revealed grating within the sheath and edema of the surrounding tissue. This condition may account for residual pain following a Colles' fracture.

Calcareous Tendinitis. The occurrence of this condition in the capsule of the shoulder was discussed under "The Painful Shoulder." Although common there and rare elsewhere, it may occur in many areas and cause acute pain, often simulating acute gouty arthritis. One case involving a flexor tendon over a distal phalangeal finger joint healed completely on rest alone, with virtual disappearance of the calcium deposit.²⁰⁰⁰ Another "accumulation of calcium matter appearing in the area of the flexor tendons of the foot" was described.¹⁴⁸¹

In 15 patients with calcific deposits occurring about the wrist and palm, eight were on the ulnar side and five on the radial side of the wrist, and two in the palm of the hand. All complained of severe pain with sudden and recent onset. The diagnosis was established by roentgenograms which suggested that the deposits were in the tendon sheath, bursae or ligaments. None gave a history of injury. Three developed calcific bursitis of the shoulder simultaneously or shortly afterwards. The prognosis is excellent, the condition being self-limiting and the recovery spontaneous. Immobilization or infiltration with procaine may give comfort while the process is running its course.¹⁷⁹⁷ [As in shoulder involvement, x-ray therapy is often helpful in acute calcific tendinitis elsewhere.—Ed.] Tendinitis of the flexor carpi ulnaris without history of trauma was associated with amorphous calcium deposits in the tendon.²¹⁸⁸ Calcareous peritendinitis of the feet was described as a possible occupational disease not previously reported. It may be found in house-painters and other workers using narrow-runged ladders.¹⁸⁹⁸

Dupuytren's Contracture. Opinions again were conflicting on the value of vitamin E. Steinberg continued to attribute Dupuytren's contracture to an abnormal

use of this vitamin by the connective tissues, and reported marked clinical benefit in 37 of 40 patients treated with vitamin E. 1837 Results were similar although not so rapid in another series, which included 13 patients. 2024 But when these claims were carefully studied by another group, 12 of 13 patients showed no evidence of improvement, and the use of vitamin E was abandoned. 1897 In an instance of excessive scar tissue following operation for Dupuytren's contracture, there was marked improvement when cortisone was used as an adjunct to active elastic splinting and physiotherapy, with further gradual improvement after the hormone was stopped. 112

Synovial Cysts. Synovial cysts of the fingers are discussed under Osteoarthritis.

Rupture of the popliteal fascia may be confused with Baker's cyst 460; trauma was be-

lieved to be a factor in some cases of Baker's cyst. 536

Calcinosis. Recent contributions were largely confined to case reports. 419, 1427, 2190 It was suggested that the differences in age and sex occurrence indicate that the circumscript and universal types are two different diseases. 520 The circumscript variety usually occurs in middle or late life. The factor responsible for the deposition of calcium is still unknown; it was postulated that in calcinosis cutis circumscripta the initiating factor is vascular block by agglutinated red cells, emboli or thrombi, and that this may be precipitated by cold, trauma or spasm. 520 In a 40 year old man with x-ray findings of multiple disseminated calcinosis, surgical treatment was found to be satisfactory provided all calcified material was removed. 220 In one patient, calcinosis cutis circumscripta was associated with Raynaud's disease. 1618

The universal type usually occurs in the first two decades of life, and involves skin and subcutaneous tissues, and sometimes tendons, nerve sheaths, muscles and fascia. An extreme degree of calcinosis interstitialis was observed in a patient with scleroderma with deposits in shoulders, elbows, hips, knees, ankles, spine, tendons and ligaments. 1424 Another patient showed numerous areas of calcification in soft tissues associated with gross destruction of the distal phalanges of the hands. 170 The x-ray diffraction pattern of calcific material from various locations was that of apatite. 1835 Symptomatic treatment included prevention of secondary infection in areas of ulceration, protection of the hands from cold, sedation and, if necessary, curettage of the deposits. 1829 A ketogenic diet did not affect the progress of the disease in one patient. 1427

MYOSITIS AND MYALGIA

Myositis Ossificans. In a group of 1,500 cadets, 1 per cent of those playing football were affected by myositis ossificans. The condition begins as an inflammatory reaction in response to hemorrhage produced by trauma. The most constant symptom is pain, which may be brief, persistent or progressive. The first physical sign is a doughy swelling which increases in size and hardness. Calcification may be seen in x-rays one to four weeks after the injury. The lesion was described as a spurious fibrocartilaginous tissue reaction to trauma, with eventual endochondral ossification. In one case, operative trauma was the precipitating factor. The gluteus muscles. Several atypical cases were reported. One of the gluteus muscles. Several atypical cases were reported. The locases, complete relief of pain resulted from x-ray therapy. As surgery is frequently followed by recurrence, a trial of x-ray therapy is justified.

Generalized Myositis Fibrosa. Only 13 cases have been reported previously. The onset is insidious, usually with stiffness in the legs, arms or back. Remissions and exacerbations may extend over many years, but the course is progressive, with contracture of the muscles involved. Pain is absent, and the affected muscles feel doughy, boggy, firm, or like a sandbag. Muscle biopsies show degenerative, inflam-

matory and fibrotic changes. 1978

Tropical Myositis. The pathogenesis is uncertain. In a patient with femoral thrombosis, pus aspirated from the thigh was typical of that seen in tropical myositis. Interference with blood supply, demonstrated in this patient at operation, was suggested as the cause of some cases of tropical myositis. 626, 627

Clostridial Myositis. Sixteen different species of anaerobic organisms were

found in specimens from 110 cases of clostridial myositis. 1867

Epidemic Myositis or Myalgia: Epidemic Pleurodynia: Bornholm Disease. Several more epidemics were reported. 364, 542, 543, 759, 812, 921, 980, 1570, 1767, 2017 In one instance eight members of the same household were stricken within one week. Prodromal symptoms were head colds, headache, anorexia and myalgia. All of 114 cases had the typical onset of severe paroxysmal pain in the upper abdomen or at the costal margin. Lymphadenopathy seen in this series had not been previously described. 548 Complications were pericarditis, orchitis, and involvement of the central nervous system. 543, 980 In one epidemic the patients had pleurodynia and cervical myalgia simultaneously. It was suggested that these are variant forms of the same infectious process.812 Epidemic myalgia affecting the trapezius muscle was said to differ from Bornholm disease. It affected only one muscle, with persistent and severe pain which sometimes radiated to the occiput or down the arm.2177 An epidemic of acute lumbar pain, with fever, headache and splenomegaly, seemed to resemble epidemic myalgia; however, the patients were found to have infectious mononucleosis. 618

Symptoms of myalgia resembling those of Bornholm disease occurred in laboratory workers investigating Coxsackie virus 2. This virus was isolated from the nasal washings and blood of a patient with Bornholm disease. The presence of complementfixing and virus-neutralizing antibodies in the blood of patients suggested that some of the epidemics were associated with infections by Coxsackie virus 1 or 2, or closely allied viruses.841 However, in a group of suckling mice infected with Coxsackie viruses, myositis was not a constant finding, but it did occur in mice infected with other types of virus. 1522 Efforts to isolate virus from material collected during an epidemic in Boston were initially unsuccessful by egg-sac and mouse inoculation methods,843 but later the intracerebral inoculation of day-old mice with throat washings resulted in isolation of four strains of virus; an antigenic relationship between two of these strains and the Coxsackie group of viruses was demonstrated. A rise in specific neutralizing antibodies was demonstrated in the patients from whom they were isolated and in other patients with epidemic pleurodynia, indicating "that these viruses are of human origin and played an etiologic rôle in the epidemic." 2151 [The evidence is impressive.—Ed.]

Myalgia. The terms "myalgia," "myalgic lesion" and "myalgic spots" were used by some to designate part of the symptom complex of fibrositis. 1054, 1055 Others employed the terms myositis or myalgia when acute symptoms were localized to the region of muscles rather than of joints. Short discarded these terms in favor of "arthralgia" and "arthralgia group," but in some patients with tender, slightly swollen lumbar muscles, fever, leukocytosis and elevated sedimentation rate, a diagnosis of myositis seemed justified. Epidemic myalgia was considered a separate entity. 2056 The syndrome of acroparesthesia was attributed to an idiopathic myalgia of the elbow, affecting the origins and heads of extensors or flexors of the wrist and hand. The injection of a few cubic centimeters of procaine "cured the condition without delay." 858 Myalgia was said to be a common symptom of amebiasis. In 10 patients, treatment

of amebiasis was followed by marked improvement of myalgia, arthralgia and rheumatoid arthritis. 2256 [Intervals between treatment and the improvement of rheumatic symp-

toms were frequently months or years.-Ed.]

In the diagnosis of painful musculoskeletal disorders it was found that routine digital palpation of the affected parts may be inadequate and sometimes misleading. To provide more accurate and helpful information, supplemental clinical aids were described. Among them were differential palpation, quantitative palpation with a pressure gauge, use of saline and procaine injections for evaluation of tenderness, and qualitative analysis of the pain. 1942

Fibrositis

Fibrositis was rightly designated as the most controversial condition in the purview of rheumatism.⁴ Almost all are agreed that it is not a single disease entity and that the various types of rheumatism which hide behind the name must be differentiated.^{993, 2086} It was defined as a mesoblastic tissue reaction brought on by different causes, known and unknown,¹⁰⁸⁴ and considered a symptom-complex rather than a well defined disease.^{500, 1055} Many considered the term unsuitable,²³⁶ "a convenient label or diagnostic refuge," ²⁰²⁵ "that dangerously embracing term." ⁴⁴⁹ Primary fibrositis was considered an "imaginary disease," ²⁸² and the term was discarded by Short because of the unwarranted implication concerning its pathogenesis. ¹⁸²⁸

Incidence. Reports on incidence continued to show great variance. In the United States the average incidence of nonarticular rheumatism among patients attending arthritis clinics was approximately 30 per cent. The incidence of fibrositis at a U. S. Army Rheumatism Center was 13.4 per cent. In Great Britain it was estimated that there are over 1,000,000 sufferers, and that fibrositis comprises more than 75 per cent of the rheumatic disorders. Of the rheumatic cases in the British Expeditionary Force to France (1939), 70 per cent were fibrositis. In the Middle East it was the chief cause of frequent and prolonged hospitalization. It was the most frequent cause of backache in general practice. The incidence was highest at the working age. If The discrepancy in incidence in different countries emphasizes the need for a better classification on an etiologic background. It is evident that in some statistics, "fibrositis" included all forms of nonarticular rheumatism; in others, it applied only to certain subdivisions. In the U. S. Army, fibrositis did not include psychogenic rheumatism, whereas in the British Forces it did.—Ed.]

Etiology. The cause of fibrositis remains controversial. No one has conclusively demonstrated that the lesion is inflammatory. 1979 Most agreed that the syndrome may be caused by many factors, and the relation to trauma, infection, exposure, fatigue, and to vascular, metabolic, postural, occupational and psychogenic factors was discussed. 55, 286, 366, 360, 429, 479, 1821, 1828, 2025, 2026 An explanation given by Himsworth (quoted by Copeman) 348 was that the syndrome has its basis in a chain of physiologic processes which can be interfered with at any point to produce the same impairment of bodily function. The same syndrome may thus arise from different causes.

The concept of focal infection had little support, 346, 2038 but some still felt that infection plays a part. 227, 1788 Kelly reiterated his hypothesis that the myalgic lesion and pain are the result of abnormal reflex activity in the deep pain nerves, regardless of the precipitating factor. 1053, 1054, 1057 One author suggested that the name should be changed to myospastic syndrome, since the mechanism involves the vasomotor effects of the sympathetic nervous system and the local and referred pain of localized muscle spasm. 1979 Copeman again suggested that the syndrome may result from abnormal

retention of fluid by fat globules confined in indistensible fibrous tissue. The origin of this selective swelling was thought to be endocrine in nature. Fibrositis from overwork was described. The stronger the contraction of muscle and the longer it continues the more ischemia results, with consequent pain. Many agreed that emotional factors play an important rôle. Fibrositis Ellman believed the syndrome to be of psychic origin in the majority of cases. All symptoms of primary fibrositis were thought to be the result of articular disorders (largely internal derangements) at the spinal joints. The syndrome was also attributed to a primary or conditioned deficiency of vitamin E. 1937

Clinical Data and Diagnosis. The chief symptoms are pain, stiffness and soreness; the usual signs, tenderness and limitation of movement. The pain varies from mild to severe, from brief in duration to intractably chronic. 1056 The usual clinical features were described. 41, 306, 616, 1247, 1821, 1828, 2036

Division into five classes-intramuscular, periarticular, bursal and tenosynovial, subcutaneous and perineuritic-was considered most valuable.2006 Fibrositis may cause a variety of somatic complaints, headaches, pleurodynia and pain in the abdomen, shoulder, forearm and hand. 1053 The most frequent sites were the lower back and the gluteal, neck and shoulder areas. 1477, 2038 Fibrositis was held responsible for the scapulocostal syndrome, which should be considered in all shoulder girdle complaints. 1890 In a patient with poliomyelitis, fibrositis was absent on the involved side and present on the uninvolved side.2178 Fibrositis was said to be the cause of "cracking joints," where the sound is produced by the stretching of constricted inflamed fibrous tissue.227 The only objective sign of the disorder lies in localized trigger points which are sometimes palpable in the form of nodules,846 but it was felt that nodules are by no means constant in location and probably represent muscle segments in spasm.1979 Inability to feel such nodules was blamed on faulty technic. Nodules were said to give rise to referred pains, superficially identical with referred visceral pains, but not initiated by visceral disease.1537

Differentiation from early rheumatoid arthritis, mild osteoarthritis and psychogenic rheumatism is the chief problem.^{826, 1247} Neuritis, intrapelvic disorders and disc lesions must also be considered.²⁰³⁵ The differentiation of interstitial neuritis was discussed.¹⁰⁸⁷ Primary fibrositis was considered the chief rheumatic disease from which psychogenic rheumatism must be differentiated.^{852, 1828} Phenobarbital relieved the psychogenic group but not those with primary fibrositis.²⁹⁸⁷ Others found that a history inquired into with sufficient curiosity would distinguish between them.¹⁸²¹ A simple pressure gauge was designed to supplement the usual routine digital palpation of painful areas, and other supplementary clinical aids were described.^{1941, 1942}

Pathology and Laboratory Data. No pathologic lesion has been generally accepted. Most consider that the lesion is not inflammatory but that the pathologic changes are chiefly a chemical, chemicophysical or enzymatic disturbance which alters the physiology of the tissues involved. Muscle biopsies failed to reveal any evidence of inflammation. Pro No pathologic difference was found between normal muscle and a muscle with altered quality due to hyperfunction. Pro In a patient with extreme pain and spasm in the lumbar area who died from endocarditis, postmortem sections of bone and muscle showed no abnormality. Pro No biochemical abnormalities have been demonstrated in the syndrome. The blood vitamin E level is usually normal. Plasma viscosity was normal.

Treatment. Recommended forms of treatment often reflected the varied concepts of etiology. It is most important to reassure the patient that he is suffering from a benign discomfort which does not lead to total or partial disability.1821 The word arthritis must be avoided.1558 The treatment of fibrositis is supportive and symptomatic. Moderate activity is often advantageous, with added daytime rest. 336 The value of physical methods of treatment was generally accepted. 65, 998, 1380, 1672, 1821, 2178, 2252 Simple home measures of physiotherapy were stressed. 1063, 1247, 2066 Injection of local anesthetics was helpful, 616, 1020, 1224, 1821 but was disappointing in chronic cases. 2085 Injections should be used only when true trigger points are found, since diffuse lesions respond poorly.682 Nodules should not be broken down. 1777 Ten patients treated with Intracaine in oil obtained complete relief, and the results were more lasting. 1201, 1940 Steinbrocker, while recognizing the value of procaine injections, indicated their limitations and listed these pitfalls in their use: errors in diagnosis and localization of pain, failure to recognize and correct causative or contributory factors, and psychogenic disturbances. The use of control saline injections was often helpful. 1940

In 30 patients, the combined use of salicylate with para-aminobenzoic acid gave superior pain relief.¹⁸⁷⁰ The rapid disappearance of fibrositic pain with the use of adrenaline and ephedrine creams was reported. The majority of patients remained free of pain while using the cream once or twice daily.^{838, 940} Thirteen patients said to be suffering from fibrositis all showed a satisfactory response when given various salts of glucuronic acid.¹⁵⁵⁹ Four patients with fibromyositis failed to derive any benefit from repeated administration of curare.¹²⁹² Some found vitamin E of value, ^{42, 43, 1937} but others failed to confirm these results.^{1794, 2065} Foci of infection should be treated conservatively.⁶⁰⁰ X-ray therapy was disappointing.^{236, 599} The use of antireticular cytotoxic serum in 10 patients also gave disappointing results.¹¹²⁰

Disorders of Fatty Tissues

Copeman has called attention to the fact that fat, like fibrous tissue and muscle, is of mesodermal origin and is subject to pathologic variations, the symptoms of which have often been labeled as rheumatic or fibrositic pain. His important studies on this subject were summarized in a Hunterian Lecture. It was believed that some derangements of water storage may underlie the symptoms, as nodules removed at biopsy consisted of fatty tissue confined in a fibrous compartment, swollen and under tension.

Herniation of Subfascial Fat. Detailed anatomic observations on fat distribution and on the occurrence of herniation of lobulated fat penetrating through fascial tears were reviewed. Fat herniae were classified as pedunculated, nonpedunculated and foraminal.³⁴⁸ [This material was reviewed extensively in the Ninth Review.—Ed.]

Copeman and Ackerman reported new cases of lumbar and gluteal pain due to edema or herniation of fat lobules. Others also found that abnormalities of subfascial fatty tissue constituted a significant factor in back pain. 434, 894, 1041 In the majority of patients the pain was referred, most commonly to the lower extremity. The condition was called "nodular fibrositis," and relief following the injection of procaine was a criterion for diagnosis. The pain simulating ureterorenal disease may be caused by fibrolipomatous nodules in the region of the twelfth dorsal and upper lumbar vertebrae. Removal of such nodules gave complete relief of pain in five patients. Nerve fibers not previously described were demonstrated in these nodules. 1814

Of 37 patients with fat herniation treated surgically, 34 were cured; an additional 54 were relieved by local injections.^{876, 876} Most agreed that treatment by local injection should be tried before surgical removal. Infrared heat and massage will often give relief.⁷⁶⁷

Other Lesions Occurring in Fat of Normal Distribution. Localized collections of fat occur normally in the upper dorsal region, as periarticular fat pads around the patella and in the popliteal area, and over the sacrum, in about 10 per cent of persons. Some instances of "fibrositis" in these areas may actually be due to swelling of this fat in its fibrous compartments. When 22 patients in whom this type of pain was suspected were placed on a dehydration regimen, 13 were rendered "completely free of pain for variable periods." ²⁴⁸

Panniculitis. This was defined as pain occurring in abnormally deposited fat. It was considered a common condition, frequently unrecognized, and too often labeled as psychogenic pain. The common sites affected were the upper dorsal region, upper and outer aspects of the limbs, and around the knees, elbows and ankles. It was often associated with general obesity. Dercum's disease (adiposis dolorosa) appeared to differ only in degree. Distention of the lobules in abnormal fat deposits was considered the likely cause of pain, inasmuch as no inflammatory histologic lesions were observed. Frequent association with the menopause suggested an endocrine etiology, but sodium balance, exposure to cold, and genetic factors, were also mentioned. In treatment the use of androgens, dehydration, physiotherapy and local injections was discussed.²⁶⁵

Chronic Relapsing Febrile Nodular Non-Suppurative Panniculitis (Weber-Christian Disease). In the thirty-seventh reported case, an unusual feature was the appearance of this disease in a patient with a history of rheumatic fever. This led to speculation regarding the possible rôle of free fat in sensitization and auto-antibody reactions, and the suggestion that Weber-Christian disease may be allied to the group of collagen diseases.²³⁶

Psychogenic Rheumatism

Psychogenic rheumatism was defined as the musculoskeletal expression of functional disorders, tension states or psychoneuroses, equivalent to the functional symptoms arising in other systems. Even those most skeptical of psychosomatic conceptions recognize that emotions are commonly accompanied by bodily changes. It is not surprising that skeletal muscles should be so affected. The patient aches in his limbs because in fact he aches in his mind. Dependent of the idea that rheumatism is actually present. The psychogenic rheumatism. It perpetuates the idea that rheumatism is actually present. The psychiatric diagnosis applicable to each case should be used. Others felt that the term is convenient and compact, a useful label if its limitations are understood.

Incidence. The incidence of bodily disturbances associated with states of anxiety and depression assumed almost epidemic form in Great Britain after World War I.⁷⁵⁷ During World War II psychogenic rheumatism was the most common form encountered in many hospitals and field areas ³³⁶; at the Rheumatism Centers of the U. S. Army, it disabled approximately one of every seven patients.¹⁷³ In two other groups of Army patients the incidence was 16.1 per cent ⁸⁵² and 16.5 per cent.¹⁸²⁸ In civilians with rheumatic complaints the incidence was 13.4 per cent ¹⁷³ and 7 per cent.⁸¹⁶ Of 183 adults with psychoneuroses, 47 per cent showed symptoms of muscular pain.⁴⁷⁹ By contrast, in soldiers such articular manifestations of the neuroses were placed at the end of the list.¹⁸²⁸

Clinical Data. The clinical pattern was not that of organic rheumatic disease. Most patients presented only a collection of subjective symptoms without objective manifestations. The degree of psychoneurosis varied from mild anxiety state to major conversion hysteria. Most patients had many complaints besides rheumatism. 846, 852 In 87 patients with psychoneurosis the common sites of pain were, in order of frequency: chest, lumbar area, upper and lower limbs, cervical and sciatic regions. The severity of symptoms varied widely, corresponding to the severity and duration of the mental conflict. 479 In one group of 24 women, all complained of arthralgia in the fingers and wrists. 1011 In 200 patients with chronic fatigue, 40 had symptoms of psychogenic rheumatism. Atypical neuralgia of the face, shoulder region and legs was frequently associated with aches in the low back or entire body. Poor sleep and poor sexual adjustment were the most frequent psychologic problems. Prominent was the presence of chronic resentment, of which the patient was usually totally unaware.2149 In 109 cases of chronic nonarticular rheumatism, evidence of a significant personality disturbance or frank neurosis was found in 79 per cent. Frustration and resentment were common. 500 Others stressed the absence of physical findings, 386, 2036 and the multiple associated complaints.⁶¹⁶ Varying degrees of muscle spasm may be found and may even limit joint movement.173 The patient misinterpreted sensations of pressure, tingling, numbness, etc., as pain,001 and the value placed on symptoms was disproportional to their severity. 1831

In military personnel most symptoms were in the lower extremities. A few patients presented joint limitation due to muscle spasm, and areas of hysterical anesthesia, but the examination was usually negative. 1828 In patients suffering from psychogenic backache and other muscle pains, needle electrodes in the skeletal muscles revealed a generalized and sustained increase in motor and electrical activity. 918

Etiology. Requisites for the development of a psychosomatic disorder were a psychoneurotic predisposition, an exciting emotional conflict, and restriction of outward expression of the conflict. Halliday stressed frustration and distortion of emotional drives, with a progressive increase of inner insecurity. In soldiers, the underlying factors were found to be combat fatigue; the subconscious demand for self-preservation; maladjustment to discipline, criticism and the "indignities"; homesickness, loneliness and worry. In civilians, outstanding factors were dominating and stern parents, housing difficulties, and domestic troubles, with their manifold fears and frustrations. In military personnel, direct contagion from fellow-patients was possible. 1828

It was emphasized that the pain has a physiologic basis and is not imaginary. 1821 The concept that emotional tension causes muscular tension through nerve irritability was satisfying to some. 1160 Since muscles are the means of defense and attack in the struggle for existence, internal tension is most easily released by muscular action, and if this is inhibited by repressive forces the resulting tension is felt by the individual as pain and limitation of movement, as in "psychogenic fibrositis." 1850 Others felt that the muscular tension state induced by emotional upset is essentially a pathologic condition, based on local tissue changes in the muscles themselves rather than on central alterations of perception. These pathologic tensions may be as relevant etiologically as are chill, fatigue, infection and other suspected causes. 160 Emotions may lead to muscular spasm and tension with resulting distortion or tearing of muscle fibers, 1850 or may induce vasomotor changes which bring about localized areas of ischemia 4 or elaboration of noxious tissue metabolites. 1818

Diagnosis. Physicians are familiar with psychoneurosis as it affects the gastrointestinal, cardiovascular and other systems, but the effect upon the musculoskeletal system has not been sufficiently well recognized. Differentiation from osteoarthritis and rheumatoid arthritis is usually easy, but the manifesta-

tions of fibrositis are largely subjective and the distinction is less clear. Primary fibrositis is therefore the chief rheumatic disease from which psychogenic rheumatism must be differentiated.^{173, 846, 852, 1247, 1821} Differential points in diagnosis were outlined.^{350, 1070, 1828} A diagnostic chart indicated that fibrositis puts its victims at the mercy of changes of external environment, whereas the victims of psychogenic rheumatism are at the mercy of their internal environment.⁸⁵²

Diagnosis by exclusion is dangerous, and both positive and negative evidence is necessary. 172, 616, 991, 1539 "The physician's point of view must be changed, not the history form. Interest must be taken in the lack of emotional satisfaction rather than lack of vitamins, and in focal conflict rather than focal infection." 2149 The entire examination, including laboratory and x-ray studies, must be sufficient to convince both the patient and the physician that no significant structural pathology is present. 1539, 1821

Treatment. The first move is the recognition by the physician and the acceptance by the patient that he has psychogenic rheumatism. "These miserable souls deserve something more than tonsillectomy, heat and aspirin." Sooner or later the services of a psychiatrist are usually required, 846 but such a consultation should be only on the patient's volition. Prompt recognition is necessary to prevent progression to the point of irreversibility. In the Army, treatment was generally unsuccessful once the patient had reached a general hospital; of 51 such patients, only four were returned to duty. Patients should be impressed early with the fact that they are not suffering from a disease of body or mind, but from a disorder of their feelings. They should carry on in spite of symptoms and try to cultivate the atmosphere of health. They require inner support, rather than sacro-iliac or abdominal supports.

Most agreed that treatment must be directed at relief of the emotional conflict, rationalization of the problems, and correction of the psychoneurosis. Unless these objectives are realized, treatment will be disappointing. Group psychotherapy is giving encouraging results.²⁰³⁸ It is essential to avoid the use of the word "arthritis." ¹⁵⁵⁸ Therapeutic failure will invariably follow an erroneous diagnosis. ⁶¹⁶ Proper psychiatric diagnosis facilitates the use of more positive therapy, opening the way to the patient's appreciation of the rôle played by tension and the need for adjustment. ⁸⁰⁰

TUMORS OF SYNOVIAL TISSUES

Tumors derived from synovial tissues, whether from joints, bursae or peritendinous structures, are relatively uncommon. This undoubtedly accounts for the fact that their clinical recognition is usually delayed, and that no definite pathologic classification has been accepted. With the collection of sizable series of cases of various types of tumors, definite progress in understanding of pathologic characteristics and clinical behavior is being made. Bennett 129 presented an excellent review of reactive and neoplastic changes in synovial tissues.

Hemangiomas. Two additional patients with hemangioma of the knee joint were described. Injury had occurred in each case years before. Complete recovery followed surgical removal. A vascular leiomyoma which involved the wrist produced pain that was curiously similar to uterine contractions; this was attributed to the presence of a small venule in each of the many whorls of spindle cells.

Osteochondromatosis and Synovial Chondromatosis. These were regarded as metaplasia of one form of mesenchymal tissue into other types that are embryologically closely related. ^{129, 223, 276} The condition is characterized by the spontaneous formation within the synovial cavities of loose bodies. These bodies consist of viable hyaline or fibrocartilage, and in the more common osteochondromatosis have a nonviable osseous core. Increase in size and density of bodies, without change in number or position, was observed in x-rays over a 10 year period. ²²³ The condition is definitely benign and produces no characteristic symptomatology. Of 104 cases, 79 were in males; a history of related trauma was obtained in about one-half of the patients. The knees were involved in 73 patients, the elbows in ^{22,1456} Involvement of the shoulder and ankle was less common. ^{223, 276} Surgical removal of loose bodies to avoid mechanical damage to cartilage, and synovectomy when practical, were recommended. ¹⁴⁵⁸

Pigmented Villous and Villonodular Synovitis. This designation, proposed by Jaffe, Lichtenstein and Sutro in 1941, to supplant such terms as xanthoma, xanthogranuloma and giant-cell tumor, has been widely accepted. Some also accepted the concept that this condition is not neoplastic but inflammatory in nature. 160, 711, 1212 Bennett 129 placed these in a group intermediate between clearly defined reactive entities and neoplastic entities, and after careful analysis concluded that many of the histologic characteristics were similar to those encountered in recognized neoplasms

of synovial origin. Pigmentation may not be present. 160

In five patients, the knees were affected in four and the ankle in one; in one patient both knees were involved. Definite injury preceded symptoms in only one. Pain and limitation of motion, in addition to swelling, were present. Effusion was out of proportion to subjective symptoms. **II X-rays were of limited value in establishing the diagnosis, which can be accomplished only by microscopic examination of tissue. **III Attempts at surgical removal were usually incomplete and followed by recurrence. Roentgen therapy appeared to exert a favorable influence **III response was rapid in the highly cellular early phase, but was less marked as duration of the disease increased. Following arthrotomy and biopsy to establish the diagnosis, irradiation was regarded as the treatment of choice. **III regions on the patients of th

Giant-Cell Tumor of Tendon Sheaths. Referred to as benign synovioma. xanthoma and tendon sheath myeloma, this slowly growing tumor is characterized histologically by large numbers of multinucleate giant cells, certain lipid-laden cells, and frequent collections of macrophages containing hemosiderin pigment. These cellular components are supported by a dense stroma of fibroblasts and collagen. These cellular components are supported by a dense stroma of fibroblasts and collagen. These cellular components are supported by a dense stroma of fibroblasts and collagen. These cellular components are supported by a dense stroma of fibroblasts and collagen. These centered shady of the histologic variations in 42 cases, and concluded that they represented behavior characteristics of the reticuloendothelial system; since they were centered around blood vessels, the tumor was classified as a sclerosing hemangioma. Bennett 129 noted that pigmented villonodular synovitis in joints was quite similar to the giant-cell tumors of tendon sheaths both in morphology and in clinical appearance, and suggested that the two types of lesions represent identical processes in synovial tissue from two anatomic locations.

In addition to individual case reports, 1298, 1988 a series of five cases 1213a and one of 30 cases 1982 were reported. Age incidence was chiefly between 10 and 60 years. The tumor most commonly arose from the flexor tendons of the fingers. A rare instance of xanthomatous tumor having the essential histologic characteristics of giant-cell tumor, which recurred after local excision and eventually metastasized widely, illustrated the problems of classification. Eennett 129 believed that in such cases, appropriate evaluation of the initial growth will usually reveal its cancerous qualities.

Xanthoma. This tumor was usually included in the preceding classifications. Most agreed with Stewart 1962 that there was no such thing as a specific xanthoma cell; the term implied a mass of cells which had phagocytosed cholesterol esters. Two cases of xanthoma of the Achilles tendon were reported.600

Synovial Sarcoma (Malignant Synovioma). Experience with 60 cases at a cancer center was reviewed by Pack and Ariel.1518 These cases represented 8.4 per cent of 717 patients who had malignant neoplasms arising from somatic soft tissues. The average age was 36 years, with 60 per cent occurring between 15 and 40 years. Trauma, usually of a severe grade, was related in nine patients, and in fact a mass had appeared in five immediately after injury. Three of the cases were thought to have arisen from benign tumors, and one occurred in a two week old child, suggesting a possible congenital origin. The knee, foot and hand were most frequently involved. The average duration of symptoms before adequate treatment was instituted was 22.8 months. The usual symptoms were a mass (in 80 per cent) and pain (in 40 per cent), but not necessarily both. There was no characteristic roentgen appearance. Metastases were most frequent in the lungs, regional lymph nodes and bone. Thirtyeight patients had primary recurrence following local resection in an average of 15.3 months, and 16 developed a secondary recurrence in an average of 11 months more. Of the 60 patients, 14 were alive and free of the disease an average of seven and onehalf years after treatment, with a survival rate of 23.5 per cent in 34 patients who were adequately treated and followed.

Bennett ¹²⁸ analyzed data on 32 specimens received at the Armed Forces Institute of Pathology and illustrated the differentiation from benign lesions and the variation among malignant lesions. Most of these tumors were adjacent to but not in the joint cavities. They seemed to arise most often in the popliteal space or in Hunter's canal; only five were associated with a history of definite trauma. Thirteen patients were known to have had metastases, while three more had local recurrences. Muirhead, Kreissl and Gordon ¹⁴⁴⁶ reported eight additional cases, and four "relatively benign synoviomas" which illustrated difficulties in histologic differentiation. There were other case reports.^{484, 803, 1318, 1911, 2173} "It is exceedingly difficult to establish the diagnosis of synovial sarcoma by any means except microscopic examination of the suspected tissue." ¹⁸¹⁸ The consensus regarding treatment was well expressed by Bennett ¹²⁹: "The known behavior of these tumors indicates the necessity for early and complete extirpation, even when this means an extensive operation. Cures are seldom obtained by local excision, and irradiation appears to have little, if any, value."

ARTICULAR DISEASE ASSOCIATED WITH PRIMARY BONE PATHOLOGY

Clubbing of Fingers and Hypertrophic Osteoarthropathy

While hypertrophic osteoarthropathy may occur as a feature of any variety of clubbing, 207 it was considered important to differentiate the generalized osteoarthropathy from clubbing alone, since the former was so often associated with pulmonary neoplasm. 209 Attention was again directed to arthralgia as the earliest symptom of intrathoracic disease, and to pulmonary malignancy masquerading as arthritis (usually resembling rheumatoid arthritis, occasionally rheumatic fever) for months before the true condition was recognized. 252, 1309, 1043, 2043 One group of investigators saw seven such patients in five years; in five, joint pains appeared to have preceded clubbing of the fingers. In three, treatment for arthritis had preceded by several months the recognition of the underlying pulmonary lesion. 212 Berg 134 found 15 such cases in the literature and added brief case reports of five more. Most commonly involved were knees, ankles, wrists and the shafts of long bones. Effusion as well as arthralgia was noted.

It was stated that the associated synovitis presented no distinguishing histologic characteristics. Several commented on the relief of articular symptoms within a few hours or a few days after resection of pulmonary tumor. 184, 858, 918, 1648

Clinical Data. Finger-clubbing was usually asymptomatic. The first sign was increased fluctuation of the nail-bed, followed by thickening of fibroelastic tissue at the base of the nail, which resulted in the filling-out of the angle between the nail and the basal tissues.^{207, 1240} "The chief component of clubbing is an increase in connective tissue in the clubbed segment." ¹²⁴⁰ Alterations in curvature of the nails then occurred. "The changes then progress to hypertrophic osteoarthropathy." ²⁰⁷ But in a patient who developed both conditions within one month, definite x-ray changes in the bones preceded clubbing.⁶¹ In hypertrophic osteoarthropathy, the pathologic process is essentially a chronic proliferative subperiosteal osteitis, with successive

thin layers of new bone formation just beneath the periosteum. 2043

The numerous diseases with which this process may occur were again listed.²⁰⁷ Unusual clinical features described include severe clubbing of fingers and toes in a two year old child who had been sick with empyema for three months ⁶⁸⁵; very advanced clubbing, periostitis and severe bone demineralization in a child with bone tuberculosis ¹¹¹⁷; association with infectious hepatitis ⁹⁷¹ and leukemia ²⁰⁴³; and a syndrome combining the clubbing of digits (with or without osteoarthropathy), metaplasia of the bladder, and mucous diarrhea.²¹²⁷ Gynecomastia was again noted in association with pulmonary tumor and osteoarthropathy.^{164, 562, 912} Marked soft tissue swelling of the wrists, in addition to the usual signs, occurred in a patient with tetralogy of Fallot without lung disease or infection. The swelling of the right wrist subsided markedly when circulation of the right arm was impaired by shunting the right common carotid artery into the pulmonary artery.¹³⁶² Acquired clubbing was

not always associated with ominous disease.971

Pathogenesis. The fundamental cause of clubbing remained the subject of conflicting theories; factors considered important were increased blood flow and local tissue anoxia. Increased vascularity about clubbed fingers, particularly in the ungual processes, was demonstrated by infrared photography and postmortem arteriograms, 202 but by means of actual volume measurements, increased blood volume in the venous plexuses was found to be a component only in cases with congenital heart disease.1240 Mauer 1828, 1324 invoked intravascular rouleau formation to explain older concepts of "toxemic" or "infectious" factors in terms of tissue anoxia. Such rouleau formation has been observed in diseases characterized by an accelerated sedimentation rate and alterations in plasma proteins, and would result in a reduction of the effective diffusion surface per unit of hemoglobin. Many of the rouleaux may escape through arteriovenous anastomoses without diffusing out their oxygen content. Mauer concluded that "rapid rates of blood flow and low tissue oxygen would provide the same mechanism for clubbing in chronic infections, neoplasms, or metabolic defects leading to abnormal fibringen and globulin levels, as in the classical cases of arterial anoxia." Exceptions were promptly noted.207, 912, 2127 Bloom 164 reported a case of bronchogenic carcinoma with metastasis to the pituitary gland, and reviewed previous implications of the pituitary gland as the source of hypertrophic pulmonary osteoarthropathy; overstimulation of the anterior pituitary by the metastatic lesions was suggested as the cause of osseous changes in this case.

Idiopathic Type. In contrast to the acquired or secondary type of this disease, the idiopathic type received scant attention. Hereditary clubbing of the digits was described in two families.³⁹⁹ Camp and Scanlan ²⁷⁰ stated that 3 to 5 per cent of all cases of osteoarthropathy are idiopathic, and added four cases (one atypical) to 21 proved and seven possible cases reviewed from previous reports. The condition occurred chiefly in males and often showed a familial incidence. Onset was at puberty,

with enlargement of hands and feet, joint symptoms and, at times, effusions into ankles, knees and wrists. It progressed slowly or not at all. Resemblance to acromegaly was superficial, and x-ray findings permitted clear differentiation.

Sarcoidosis

Interest in and clinical awareness of sarcoidosis was reflected in numerous publications; only a few can be mentioned. The protean nature of sarcoidosis and its diverse clinical manifestations have led to many different names and concepts of the disease (Ninth Rheumatism Review). The following definition was agreed on at a National Research Council Conference in 1948: "Sarcoidosis is a disease of unknown etiology, characterized pathologically by epithelioid tubercles, with inconspicuous or no necrosis, occurring in any organ or tissue, and by the frequent presence of refractile or apparently calcified bodies in the giant cells of the tubercles. The lesions may be replaced by fibrosis, hyalinization, or both. Clinically the lesions may be widely disseminated. The tissues most frequently involved are lymph nodes, lungs, skin, eyes. and bones (especially of the extremities). The clinical course is usually chronic with minimal or no symptoms. However, there may be acute phases, characterized by malaise and fever. There may be symptoms referable to the tissues and organs involved. The tuberculin test is frequently negative. Plasma globulin is often increased. The outcome may be clinical recovery without gross or radiologically visible residuals, or it may be impairment of the functions of the organs involved, or a continuous chronic course of the disease." 879

Incidence. Of 350 patients with sarcoidosis observed in military personnel during World War II, a heavy preponderance had been born in the southern or southeastern United States, and in rural areas.¹³⁶⁹ The higher incidence in Negroes was again noted.^{942,959} There were about 20 times as many cases per 100,000 in Negro inductees as in white.¹³⁸⁹ In different series, the percentage of Negroes was: 81 per cent of 52 cases (New Orleans ⁹⁴²), 79 per cent of 52 cases (New York ¹⁶⁸⁰), 58 per cent of 300 cases (U. S. Army ¹⁶⁷⁸), and 83 per cent of 94 cases (Baltimore ⁵⁵⁴). Sarcoidosis occurred in two unrelated families (both Negro), affecting at least five and possibly eight of 13 siblings.¹⁶⁹³

Clinical and Pathologic Data. In addition to many case reports, several excellent reviews appeared. 40, 270, 284, 591, 728, 1680 Particularly noteworthy was the analysis of 300 consecutive cases from the files of the Armed Forces Institute of Pathology. 1678 Of 258 patients who presented symptoms, 221 complained of enlarged lymph nodes; only seven presented swelling of bones and joints of the extremities. Of 195 with organ involvement (other than lymph node), 34 (17.4 per cent) had bone lesions. This series included 22 autopsied cases; sarcoidosis was unsuspected until autopsy in 14, and in only three was death unequivocally due to sarcoidosis. Three of the 22 had associated sarcoidosis and tuberculosis, and two more showed abacterial caseating lesions of the adrenal glands, with clinical Addison's disease. In the histopathologic material, "fibrinoid necrosis, usually distinguishable from the caseation of tuberculosis, occurred in 35 per cent."

In eight series of cases, 504, 820, 918, 942, 1144, 1388, 1678, 1690 the frequency of bone involvement ranged from 10.5 to 21.4 per cent; the average for the total of 617 cases included in these series was 13.0 per cent. Holt and Owens 918 described in detail the osseous lesions of sarcoidosis, with their peculiar predilection for the phalanges. They found the diffuse, coarse, reticular type of bone destruction with its lacelike roentgen appearance much more common and characteristic than the circumscribed punched-out lesions. Joint lesions were described in detail in only one patient, a six year old Cuban boy who presented a picture simulating Still's disease of three years' duration. While lymph node and skin biopsies showed typical histologic le-

sions of sarcoid, synovial biopsy showed only a nonspecific inflammatory process. The child subsequently died of tuberculosis.²⁸⁶ [There is nothing in this well documented report to indicate that the child did not have two diseases, sarcoidosis and rheumatoid

arthritis .- Ed.]

Etiology and Pathogenesis. No definite etiology has been established. Further evidence of its close association with tuberculosis was presented.^{268, 445, 1508, 1788} Others suggested that it represented a morphologic expression of a hyperimmune state, ²⁰⁴⁰ or a common tissue response to diverse irritating agents.^{879, 881} Skin tests with lepromin yielded no evidence that sarcoidosis is a modified or attenuated form of leprosy.^{789, 2142}

Treatment. Massive doses of calciferol or dihydrotachysterol appeared to improve both skin and systemic lesions in five patients (one with bone involvement). Toxic reactions occurred in all patients, but no permanent damage was detected.³⁸¹

Gaucher's Disease

This rare, often familial disease is distinguished by the presence of characteristic lipoid-laden cells in the organs of the reticuloendothelial system. The bone lesions are due to infiltration and replacement of bony trabeculae by these kerasin-bearing cells; the severity of bone lesions and development of skeletal symptoms appear to increase with duration of the disease. Repeated attacks of low back pain may be the first complaints; the patient may enter the hospital with a spontaneous fracture or a

deformity of femoral head.728

Several excellent reviews of the radiologic features of the osseous lesions appeared.^{677, 1143, 1423, 1425} The findings must be differentiated from tuberculosis, osteomyelitis and rheumatoid arthritis. Additional cases presented x-ray and clinical findings typical of Legg-Calvé-Perthes disease.^{435, 1425, 1425} and five cases appeared as aseptic necrosis of bone.⁵⁰ Roentgen signs of bone formation in the medullary cavity of long bones, as distinct from the destructive lesions, were at times of diagnostic value.²¹⁸⁹ Bone lesions were usually multiple, and bone-marrow aspiration was often helpful in establishing the diagnosis. Osseous changes were seen in patients without splenomegaly.¹⁴³¹ Splenectomy neither prevented the subsequent development of bone lesions nor affected their progression.^{485, 728}

Osteochondritis

Osteochondritis of Growth Centers (Epiphysitis). The custom of using a different eponymic designation for each anatomic location of this condition has provided the clinician with convenient labels but has not aided clarification of etiology and pathogenesis. While any growth center in the body can be affected by this disturbance in bone development, the most common sites are spine, hip and knee. Osteochondritis of the spine is discussed under Backache and Sciatica.

Hip. In Legg-Calvé-Perthes disease, the primary disturbance is in the femoral capital epiphysis and upper portion of metaphysis of the femur. The disease is self-limiting, as the aseptically necrotic bone is replaced by granulation tissue and new bone. However, during this plastic phase the femoral head is vulnerable to the deforming effects of pressure. Pathologic changes noted in material removed at operation in 33 cases showed such necrotic and pressure changes, plus evidence of frustrated attempts at healing; the findings were regarded as those of disturbed local metabolism rather than those of trauma or infection. By injecting alcohol around vessels and nerves supplying the femoral head in young rabbits, lesions similar to

those of the disease in humans were produced.¹⁶³⁶ Multiple etiologic factors producing the same anatomic and clinical entity were suggested.^{458, 827} The influence of heredity was again recorded.¹³³⁴ In one family 28 of 88 persons in five generations were affected; the trait behaved genetically as a simple dominant, but with variable expressivity.¹⁹⁵⁶

This disease may remain undiagnosed until adult life. In five apparently normal men who developed hip disease after injury or a period of unusual activity, x-rays revealed Legg-Calvé-Perthes disease. 1996 Since routine views of the hip joint may fail to reveal defects as large as one fourth of the femoral head, "four-plane" filming should be used routinely. 144 Enforced recumbency with elimination of all weight-bearing until regeneration of the head is completed was again advocated. 19, 1571 An ingenious sling that will accomplish this purpose without casts or splints while allow-

ing the patient to get about on crutches was described.1878

Knee. Usually included with osteochondritis of growth centers has been Osgood-Schlatter's disease, characterized by painful tibial tuberosities in the adolescent. After careful study of variations in anatomic and radiologic development of the tibial tuberosity, Hughes **6 felt that the pathologic change was in the ligamentum patellae rather than in the apophysis, and regarded the essential lesion as "tendinitis" rather than "epiphysitis." The condition is not rare in youths engaging in vigorous exercise; 13 cases were seen in a nine week period at a large Naval-recruit training center. 1182 Osteochondritis of an accessory center of ossification at the inferior pole of the patella (Larsen-Johansson's disease) may be associated. 2200

Osteochondritis Dissecans. Osteochondritis dissecans is a noninfectious aseptic necrosis of subchondral bone leading ultimately but not invariably to an osseocartilaginous sequestrum into the joint. It is essentially a disease of youth. In a series of 42 cases, 60 per cent gave a history of trauma; 33 involved the knee, 27 of these affecting the medial femoral condyle. Postmortem examination of an affected knee showed only a slight discoloration of the cartilage without a break in its surface but with an easily removable sequestrum beneath. center was formed of necrotic bone with a loss of lamellar substance. 1170 The usually accepted predilection for the knee (85 per cent)2008 was not borne out by experience in England. 1685 There the elbow was more frequently involved, with the capitellum the most common location and the head of the radius a less frequent site. 1685 Other series of elbow-region involvement were reported. 483, Osteochondritis dissecans around the ankle is not uncommon, the talus being the usual site of the lesion. 1179, 1648, 1852, 2091 The condition also occurred in the head of the femur, 117, 558 the phalanx of the great toe 1179 and shoulder 1179, 1407; it may, however, occur bilaterally or affect multiple joints in the same individual. 831, 822, 888, 1110, 1179, 1497

A medial femoral triangle of translucence which can be mistaken for osteochondritis dissecans is normally present in many radiographs of the knee. It is due to the variation in width and shape of the lower medial border of the inner femoral condyle as it sweeps upward and laterally. The medial aspect of the intercondyloid notch is thinner in some individuals, giving rise to this peculiar triangular zone of decreased density. 2148

The cause remains obscure, possible etiologic factors being trauma, infection, impaired nutrition, and embryonic or neoplastic abnormality.²⁰⁰⁸ Development and progression of lesions were described in detail.^{867, 1179} Conservative treatment may be adequate in young individuals, but removal of fragment or fragments is indicated when symptoms persist.^{117, 1688, 1882, 2008}

Aseptic Necrosis

Several excellent reviews of the etiology and pathology of aseptic necrosis were published. 982, 1566, 1739 Any process or injury which produces occlusion of blood supply to bone may result in aseptic necrosis. The majority of cases resulted from trauma to the blood supply following fracture of the femoral neck, dislocation of the hip, dislocation of the capital epiphysis of the femur and vigorous attempts at manipulative reduction or surgical correction, or following arthroplasty or vigorous stripping of fragments in surgical treatment of fractures. The nontraumatic cases followed Legg-Calvé-Perthes disease, decompression sickness, x-ray treatment for malignancy of the pelvis, occlusion of blood vessels by embolism, thrombosis or arteriosclerosis; some had no apparent cause. Because of weight-bearing, collapse of the femoral head with consequent secondary disabling osteoarthritis was an important problem. In an unusual case of aseptic necrosis with acetabular involvement the x-ray changes resembled tuberculosis of the hip. 1789

Since the usual methods of recognition of aseptic necrosis (x-ray, bone biopsy with histologic study, supravital staining, or injection of fluorescein) were inadequate, injection of P³² was utilized to determine whether the bone of the femoral head was viable. In 13 fractures of the femoral neck in humans, when P³² was injected and bone biopsies were obtained from the capital fragment and the greater trochanter, three patients were demonstrated to have interference with blood supply to the femoral head. Two of them developed clinical evidence of aseptic necrosis, and the third (in whom the isotope ratio was more normal) had evidence of localized aseptic necrosis. This method may enable the surgeon to determine at the time of operation whether

the femoral head is viable.2071

Treatment. According to Phemister, 1566 the best treatment for aseptic necrosis of the femoral head consisted of drilling in the region of the greater trochanter and inserting rectangular bone grafts into the head, perforating the cortex and articular cartilage. Thus revascularization and replacement of the nonvital bone, and replacement of the dead articular cartilage by fibrocartilage, were accomplished most rapidly. Horwitz, 152 in his series of 81 cases of osteoarthritis of the hip joint (16 following aseptic necrosis), obtained satisfactory results only with arthrodesis and not with vitallium cup arthroplasty. It was his opinion that early adequate treatment of hip joint lesions was necessary to prevent the development of a secondary osteoarthritis, and that surgical procedures designed to revascularize the hip were unsatisfactory. Satisfactory relief of pain in six of seven patients with osteoarthritis of the hip following aseptic necrosis was obtained with the relatively simple procedure of sensory denervation of the hip. 1462

CONGENITAL DEFECTS

Ehlers-Danlos Syndrome. Additional cases were reported of this congenital dystrophy of mesenchymal tissue, characterized by hyperelasticity of skin, hyperextensibility of joints, and a hemorrhagic tendency 1098; associated congenital cardiac anomalies were present in some. 589, 2110 In two sisters, numerous subcutaneous calcified nodules were demonstrated by x-ray. 917 In one family, 19 of a total of 47 individuals in four generations were said to have been affected. 225 In another kindred, the pedigree suggested a definite dominant inheritance. 908 Various features of the syndrome were reviewed 908, 1682 and the term "dermofragility" was suggested. 1718

Perhaps related was the condition described by Sutro. 1994 In five soldiers, overlengthening of capsular and ligamentous tissue, permitting hypermobility of bones, was apparently responsible for recurrent intra-articular effusion (three knees, two ankles). The unusual range of joint motion was well illustrated by photographs and x-rays. None of these patients showed any hyperelasticity of the skin or skeletal anomalies, and there was no family history of similar findings.

Arthrogryposis Multiplex Congenita. Sixty patients were described in whom there were joint contractions. The outstanding symptom was rigidity of one or more joints. In treatment, the best results were obtained by conservative methods, which must be instituted at the earliest possible age. Surgery was used in some patients. 1949

Arthro-Onchodysplasia. The syndrome consists of (1) deformity and luxation of the head of the radius, (2) hypoplasia or complete absence of the patellae, (3) posterior iliac spurs, (4) dystrophy of the finger nails. Two members of a family exhibiting this hereditary syndrome were reported.²¹⁸

Morquio-Brailsford's Disease. This may be confused with rheumatoid arthritis, particularly when the hands are involved. The primary disorder is an abnormality of development of skeletal tissues, which may vary in severity from changes incompatible with life to mild deformities of the trunk or limbs. It is characterized by multiple irregular centers of ossification in the epiphyses and diaphyses, followed later by secondary deformities and marked muscle weakness. Dwarfing was found in many cases, because of spinal changes. The hips were most frequently affected. In both cases reported there was consanguinity of the parents. 498

Congenital Contracture of the Fifth Finger. One of the most frequent of inherited digital anomalies, this condition is bilateral and symmetrical. The tendency to confuse it with rheumatoid arthritis, other arthropathies, or Dupuytren's contracture was noted. It should be recognized as a benign, nonprogressive anatomic peculiarity which requires no treatment. 1803

STRUCTURE AND FUNCTION OF ARTICULAR TISSUES

Important studies on the fundamental nature of connective tissue and its components were undertaken, by means of newly developed physical and chemical methods of investigation. Valuable reviews on the development, anatomy and physiology of joints appeared 392, 294, 395; particularly comprehensive was Gardner's, 622 with 521 references.

Basic Structure of Connective Tissue

"Connective tissue is a complex of mobile, multipotent cells, fibrous structures, and an amorphous matrix." 724 Investigation of the fibrous components and ground substance has centered largely on collagen and hyaluronic acid.

Collagen. The increased resolution obtained with the electron microscope and x-ray diffraction patterns has yielded new information concerning fine structure. 50, 124, 725, 880, 1400, 1779 Fragmentation of collagen yielded fibrils extending many microns in length and ranging roughly from 200 to 2,000Å in width. All forms of vertebrate collagen examined were characterized by very regular crossbanding, with an axial repeating period of 640 Å. [This does not imply that all collagens are identical.—Ed.] By suitable methods, a characteristic pattern of intraperiod sub-banding with at least six striations in specific positions within the main period was demonstrated. Argyrophilic fibers (by definition, reticulin) in the corium of new-born rats revealed the same cross-striation and intraperiod structure characteristic of adult collagen; with increasing age, there were a continuous decrease in the proportion of argyrophilic fibers and an increase in general fibril width. While characteristics of fibrils were the same in infant and adult human skin, infant skin had a greater amount of amorphous material. 728

The predominant fiber formed in tissue culture under certain conditions appeared under the electron microscope with cross-striations usually evenly spaced at 270 Å; larger strands with the characteristic periodicity of collagen seemed to be composed of varying numbers of these unit fibers.¹⁸⁸⁸

The chemistry of collagen was reviewed.¹⁰²⁸ The characteristic high concentration of proline and hydroxyproline in collagen was apparent in material prepared with a minimum of chemical treatment.¹⁹⁹ Collagens from several sources were found to be resistant to trypsin, chymotrypsin and papain, but were attacked by proteolytic enzymes of Clostridium histolyticum and Cl. welchii.¹⁴⁷¹ The properties of these collagenases were described.^{148, 2079} Trypsin seemed to modify collagen so that subsequent treatments resulted in degradation.²⁸⁵ The collagen content of tissues in scorbutic guinea pigs was in no instance lower than in normal animals of the same weight.⁸⁰¹

Ground Substance and Mucoproteins. The ground substance was considered a complex of acid polysaccharides and proteins (mucoproteins); it presumably was visualized as amorphous interfibrillar material under the electron microscope. Although the mucopolysaccharides of human skin were isolated and determined as averaging 24.5 mg. of hyaluronic acid and 26.2 mg. of chondroitin-sulfuric acid per 100 gm., so observations concerning the mucopolysaccharides of ground substance depended on histochemical methods. None of these, even when combined with the use of hyaluronidase, have been established as specific for chemical identification. It has seemed to many that the loose use of the term hyaluronic acid to designate metachromatic material is to be deplored, whether hyaluronidase treatment was employed or not. Actually, in the present state of our ignorance, material demonstrated by histochemical technics may properly be described only as "metachromatic" or "periodic acid Schiff positive" and nothing more.—Ed.]

Mucoproteins were also demonstrated in plasma, showing at least three components with isoelectric points more acid than that of albumin; the major one traveled with the alpha₁-globulin on electrophoresis at pH 8.4, and was increased in disease. They could be demonstrated by electrophoresis at pH 4.5. Serum polysaccharides, both with and without hexosamine, were determined in normal subjects 1822 and in patients with arthritis, cancer and bacterial infections. 1828

Hyaluronic Acid. "The occurrence of hyaluronic acid has been demonstrated by isolation and chemical characterization only in umbilical cord, synovial fluid, skin and some mesenchymal tumors. In loose connective tissue, its occurrence has been postulated from effects of spreading reaction, and recently from histological work." 1876

Modifications of the methods of preparation of hyaluronic acid with resulting increase in the viscosity of the product were reported. 744, 986, 1878 The basic unit as a disaccharide composed of acetylglucosamine and glucuronic acid was accepted, but there was disagreement as to further details of chemical structure. 744, 986, 1875 [Recently the structure of the basic unit has been proved to be beta-glucronido-1-3-N-acetyl glucosamine.—Ed.] Jeanloz 985 warned that it was unsafe to use the Hotchkiss reaction for identification of polysaccharide structure, since the reaction of compounds with two adjacent free hydroxy groups was not consistent. [This reaction is the basis for some histochemical methods.—Ed.]

Hyaluronic acid prepared from synovial fluid by ultracentrifugation always contained a constant amount of protein. Since removal of this protein led to degra-

dation, it was concluded that hyaluronic acid occurs in synovial fluid as a definite complex with protein, containing 30 per cent protein, 25 per cent glucosamine, and possibly 15 per cent of non-nitrogenous polysaccharide. Meyer, 1376 however, concluded that hyaluronic acid occurred in nature as a freely dissociable compound not chemically bound to protein. From studies on synovial fluid mucin, Ropes and co-workers agreed that evidence obtained in electrophoretic studies suggested that the polysaccharide occurs free in synovial fluid; however, the results of experiments on precipitation, filtration and viscosity suggested that the polysaccharide-protein complex is not appreciably dissociated in normal fluid. The irreversible loss of viscosity produced by high temperatures or esterification was thought to be compatible with the hypothesis that the particles of hyaluronic acid are interconnected in a micelle with a loose, spongelike structure. It is evident that some of this disagreement is due to difficulty in preparing the highly polymerized complex material without also degrading it in the process.—Ed.]

Hyaluronic acid, as it occurs in nature, was considered to have a range of molecular weights averaging about 500,000. Ogston and Stanier ¹⁸⁰⁰ studied its physical characteristics by several methods, and all of their data indicated the particles of hyaluronic acid to be large and asymmetric, with a length of 200 m_{μ} and a probable thickness of 3.3 m_{μ}. [The asymmetry has since been denied by the same workers.—Ed.] By electron microscopy, sodium hyaluronate appeared as irregular flat amorphous lakes

from which extended long, thin, branching fibrous processes. 724

Hyaluronidase and Inhibitors. Enzymes capable of disaggregating and depolymerizing hyaluronic acid are widely distributed in nature.¹³⁷⁴ Most intensively studied were those extracted from testes and those of bacterial origin. The turbidimetric and reductometric methods of determining hyaluronidase were found to agree closely.¹⁶⁴¹ The viscosity-reducing method was less reliable,¹³⁷⁶ and the mucin clot-prevention test had a high intrinsic error.¹⁸⁷⁴ Modifications to increase the accuracy and range of turbidimetric methods were presented.⁴⁴³, ⁵²³, ¹⁷⁷⁸

Further study of hyaluronidases indicated they were mixtures of at least two enzymes, one attacking the long-chain molecule of the polysaccharide, the other hydrolyzing to monosaccharides. ¹³⁷⁴ A relatively constant ratio of activity of testicular hyaluronidase toward chondroitin-sulfate and hyaluronate indicated that hydrolysis of both was attributable to the same enzyme. ¹³⁷⁹ [These observations have been confirmed in later studies. Since the same enzyme can affect more than one polysaccharide, numerous studies in which hyaluronidase was used to indicate the specificity of a histochemical method

for hyaluronic acid must be reëvaluated.—Ed.]

While hyaluronidase activity paralleled the activity of "spreading factor," correlation between spreading reaction and physicochemical methods of hyaluronidase estimation was poor.1876 The "dermal barrier," interpreted as new hyaluronic acid, was reconstituted in 48 hours after its removal by hyaluronidase. 830 Testicular hyaluronidase was reported to increase capillary permeability 502 [an effect later shown to be due to impurities in the enzyme preparation-Ed.] and the permeability of lens capsule and urinary bladder, but not to alter the permeability of muscle or skin. 1798 The spreading effect of hyaluronidase was reported to be inhibited by adrenochrome, \$10 rutin 1205 and adrenal cortical steroids (see section on The Adrenal Cortex and Rheumatic Diseases). Testosterone, estradiol benzoate, progesterone, and pregnenolone had no immediate effect.1811 ACTH, cortisone and desoxycorticosterone had no effect on the in vitro activity of hyaluronidase,649 but were reported to alter its action on the permeability of lens capsule and urinary bladder.1798 Large molecules, including chondroitinsulfate, leaf gelatin and starch, inhibited the action of hyaluronidase in increasing the permeability of fresh fascia of mice. 408 The spreading action of hyaluronidase in the skin was inhibited after administration of salicylates in several studies, 444, 782, 783, 1881 but not in others. 1001, 2018, 2014 While in vitro actions of hyaluronidase were inhibited

only at high concentrations of salicylates, ^{644, 614, 1245, 1874} they were reported to be inhibited by much smaller concentrations of gentisic acid, ¹⁸⁷⁸ a product of salicylate metabolism. [While others have failed to confirm inhibition in vitro with gentisic acid itself, there is good evidence of this effect by oxidation products of gentisic acid.—Ed.] Gentisic acid and its quinones inhibited the spreading action of hyaluronidase. ^{647, 1877}

Inhibitors of hyaluronidases from various sources have been observed and measured in human sera. A nonspecific inhibitor, usually studied by its action against testicular hyaluronidase, apparently was not an enzyme 443 or an antibody 1274 or a mucoprotein. 648 Electrophoretically it migrated with the albumin fraction. 650 It was usually found to be thermolabile. 614, 2052 Its activity appeared to be dependent on the presence of four components of complement. 1280 Activity of this inhibitor was decreased by high concentrations of magnesium and low concentration of phosphates, and evidence indicated a possible rôle of sulfhydryl groups in both the enzyme and inhibitor actions. 649 The serum inhibitor of testicular hyaluronidase was increased during menstruation and postpartum, 750 and was low in normal men of reproductive age. 643 It was elevated in some patients with infectious diseases, liver disease and cancer. 614, 696, 1876 It was reported to be decreased in animals following adrenalectomy, and to be increased by exposure to various types of stress. 671 [This topic is discussed further in the section on Rheumatic Fever.—Ed.]

In contrast, at least some inhibitors of bacterial hyaluronidases appeared to be antibodies. The inhibitors for pneumococcal and staphylococcal enzymes were thermostable.²⁰⁵² The streptococcal antihyaluronidase titer increased with age through childhood, but was relatively constant from 20 to 60 years of age,¹⁶¹⁰ and appeared as a specific antibody following streptococcal infections and rheumatic fever.^{801, 1609, 1611, 1612} [The subject of hyaluronidase and inhibitors is most confusing if certain factors are not kept in mind. The results of any study appear to depend on (1) characteristics of hyaluronic acid substrate used, (2) source of hyaluronidase, (3) method of determination employed, and (4) inhibitory action of anticoagulants or diluents. It is frequently impossible to compare

studies from different laboratories.-Ed.]

Synovial Tissues and Synovial Fluid

Anatomy. A convenient new method of injecting the vascular system with India ink in human plasma confirmed the very rich blood supply of synovial membrane, especially in the areolar areas. Lymphatic vessels were outlined beautifully by stab injections; they communicated freely with the lymph vessels of the periosteum, but none was seen in the villi. The variations in the histologic characteristics of the synovial membrane from zone to zone were confirmed. The majority of nerves to joints were closely associated with blood vessels. They arose from the nerves supplying the area and each nerve supplied a definite region of the joint, with some overlapping. Many complex endings of the Ruffini type were found in the synovial membrane, in addition to free nerve endings. Most of the nerves were of sympathetic origin, but there was a substantial somatic nerve supply. Most of the nerves were of sympathetic origin, but there was

Joint Fluid. The origin of the hyaluronic acid of synovial fluid continued to be disputed. Meyer 1874 and Gardner 822 felt that the available evidence indicated its secretion by synovial cells. Hansen, 772 however, concluded that mast cells secrete hyaluronic acid. He observed coincidental variation in the number of mast cells and the amount of metachromatic ground substance and a similar staining reaction of mast cell granules and of hyaluronic acid; and after enzymatic breakdown of hyaluronic acid in tissue, he noted that new metachromatic ground

substance appeared first around mast cells. [The limitations of histochemical meth-

ods have been indicated previously.-Ed.]

The hyaluronic acid concentration in normal cattle synovial fluid was found to be 20 to 25 mg. per 100 c.c., and in normal human fluid ranged from 80 to 150 mg. per 100 c.c. 1874 The mucin content in normal fluid from various species ranged from 0.3 to 0.8 gm. per 100 c.c.¹⁷¹⁸ Detailed studies of the characteristics of synovial mucin ¹⁷¹⁸ and of the hyaluronic acid in joint fluid 1500 appeared. The logarithm of the viscosity of the joint fluid was found to be proportional to the concentration 1630 and to the square root of the concentration 1718 of mucopolysaccharide. The viscosity of pathologic fluids was low in many cases of rheumatoid arthritis. 1620, 1630, 1718 [Joint fluid abnormalities are discussed further under Laboratory Findings in Rheumatoid Arthritis.-Ed.] Irradiation of joint fluid in vitro resulted in a decrease in viscosity, but did not alter its susceptibility to the action of testicular hyaluronidase. 1626 The fiber-forming capacity of synovial fluid was related to the concentration of the mucopolysaccharide. Testicular hyaluronidase reduced the fiber length. 788 Hyaluronidase activity could not be demonstrated in synovial fluid or tissues. 1718 It was possible to produce weak antisera to mucin 1718 [but not to hyaluronic acid.—Ed.]. Normal human synovial fluid contained no isoantibodies, and very few diphtheria-immune antibodies crossed the blood-fluid barrier in normal joints. In contrast, fluids from diseased joints contained isoantibodies and diphtheria-immune antibodies in titers approximately the same as the serum. Blood group-specific substances were virtually absent in normal synovial fluid.1825

Physiology. Several studies were concerned with absorption of dyes and of penicillin 891, 1471a from joint fluid to blood and vice versa. Absorption of trypan blue from normal joints appeared to be mainly by diffusion into the blood. 1760 The relationship of intra-articular pressure to the rate of absorption from the perfused joints of rabbits was carefully studied. As in other connective tissue, resistance to flow was found to yield suddenly at a definite pressure ("breaking point"), which was not dependent on maintenance of the circulation. Following initial injections with pressures above this point, subsequent injections resulted in a direct proportion between inflow and pressure, even at low pressures.⁴⁷⁷ Elimination of the breaking point, with increased absorption of colloids from the joint, was produced by exercise,477 and by administration of Salyrgan. 478 Increased amounts of protein were absorbed from joints infected with staphylococci or inflamed by staphylococcal filtrate. This increase in absorption was prevented by DOCA, which had no effect on absorption of protein from normal joints.476 The permeability of synovial membrane was measured by injecting phenolsulfonphthalein into the joints of rabbits and determining the speed of its excretion in urine. Hyaluronidase and DOCA each increased permeability maximally, and the effect of one could not augment that of the other. 1700 [Results of studies by this method are discussed further in the section on The Adrenals and Rheumatic Diseases.-Ed.1

Comparative changes of pH in the joint fluid and blood of dogs were studied by electrometric methods; the fall in pH following exercise, nerve stimulation or induced convulsions was slower and more prolonged than in blood. 1014, 1081 Sympathectomy was followed by a greater drop on the operated side, with very slow recovery. 1653 No change in rate of transfer of acid fuchsin from blood to joint fluid was found after sympathectomy. 804 In an electrochemical study of the synovialis in dogs, the mobility of most ions in synovial tissues appeared to be close to that in water. 1015 The action of various systems of metabolic inhibitors on the membrane potentials of the synovialis was studied. 1032 The differences of potential between synovial fluid and skin were below 5 mv. in normal subjects, and above 30 mv. in patients with rheumatoid arthritis. 1032 Following ACTH treatment, in six cases the potentials dropped

immediately, but regressed somewhat in three cases while they were undergoing treatment.

The intra-articular temperature correlated better with the activity of rheumatoid arthritis than did the skin temperature over joints. The joint temperature fell with hot packs, and rose with cold packs, diathermy, pain, apprehension, smoking, passive motion of joints and weight-bearing.⁹¹¹

Physiology of Cartilage

Chondroitin-sulfate from hyaline cartilage had a specific rotation of -30° and was hydrolyzed by testicular hyaluronidase whereas that of skin had a rotation of -55° and was resistant to testicular hyaluronidase. Since the chondroitin of cartilage could be extracted with neutral calcium chloride, Meyer concluded that it was not stably linked to protein, in contrast to that of skin and of umbilical cord, which could be liberated only by strong alkali. 1876

However, since only part of the protein of the chondroitin complex could be extracted by phenol solution, and since the electrophoretic pattern of chondroitin revealed three boundaries (chondroitin, protein, and a complex of the two), Partridge felt that chondroitin and protein were combined in vivo. The association was thought not to be a salt formation, since it took place at alkaline reactions at which both protein and polysaccharide were negatively charged.¹⁵³⁴ A new method for preparing chondroitin

from bovine tracheal cartilage was reported.480

Alkaline and acid phosphatases, as well as an enzyme most active in a neutral medium, were found in hypertrophic costochondral cartilage and periosteum.⁵⁶⁸ In the cells of articular cartilage, however, alkaline phosphatase but not acid phosphatase activity was found; lipase and indophenol oxidase activity were also demonstrated. Stored glycogen and lipid droplets appeared to be normal inclusions in the cytoplasm of human cartilage cells.¹⁴¹⁷

In patients under the age of 40 who had costal cartilage calcification, the incidence of multiple complaints was twice as frequent, and the incidence of complaints not due to apparent organic disease five times as frequent, as in patients without cartilage calcification. It was suggested that premature calcification may be evidence of a link between psychiatric and previously unrecognized endocrine disturbances.^{925, 926}

Other Studies

Growth of Skeletal Tissues. The present knowledge of the development of joints was reviewed. 305, 622 Long bone growth at epiphyses was followed by regressive changes in the cartilage, and then resorption. All three processes were enhanced by anterior pituitary and thyroid hormones and by high fat diets, and were decreased with undernutrition. With parathyroid and androgenic hormones, regression and resorption were increased whereas estrogenic substances decreased growth and resorption, but increased regression. 1842, 1844

Studies of the development of the tendons of the hand demonstrated a definite pattern of fibers connecting the dorsal extensor apparatus with the metacarpophalangeal and proximal interphalangeal joints. ¹⁰³⁶ In studies on rabbits, it was found that the entire tendon grew interstitially in length, with maximal growth near the junction of muscle and tendon. ⁸⁷¹ A satisfactory tendon sheath could be produced in rabbits

and guinea pigs with a flexible plastic (Tygon). 765

Joint Pain. The types, causes and treatment of pain in arthritis and rheumatism were discussed. 1070 Deep pain sensibility could be dissociated from both cutaneous pain and deep pressure. 1050 Kellgren summarized extensive experimental studies in humans as showing deep pain to have certain characteristics of quality, inaccurate or

diffuse localization, associated muscle spasm and susceptibility to cooling, which were different from the characteristics of cutaneous pain. The two sensibilities probably were mediated by different types of nerve fibers. The "cold pain" produced by cooling an extremity was deep and diffuse in distribution, and the deep tissues at the source of pain were abnormally sensitive to mechanical stimuli. When deep hyperalgesia was present, even slow cooling of an extremity caused severe and prolonged pain, in contrast to the analgesia which soon superseded the pain produced by cooling of a normal extremity. 1051 Articular ligaments were found to be richly supplied with nerves and highly sensitive to pain or pressure, in contrast to synovial membrane, which contained fewer nerves and was relatively insensitive, with only occasional spots that gave rise to pain. 1082

Joint Motion. The development of goniometers, their use and the methods of recording joint motions were reviewed. 1426, 1650 The value of the universal goniometer and the importance of having a single observer for closely comparable results were indicated. 838, 1426 Various modifications of older methods of measuring and recording joint motion were described, 446, 954, 2170, 2226 including a clever optical goniometer. 2170 A grip ergograph was useful in assaying and treating hand weakness and in evaluat-

ing residual disability.889

The adaptation of articular surfaces to various types of joint motion was analyzed by MacConaill.^{1266, 1267, 1268} The efficiency of saddle joints for permitting rotation combined with circumduction, and the adaptation of the trochlear surfaces of hinge joints to minimize wear, were indicated. Successive swings of a joint such as the shoulder were found to be accompanied by rotation (conjunct rotation). The muscles of a given joint were rotators to some degree, and conjunct rotation seemed to offer a means of exercising muscles that were too weak to raise the limb normally.¹²⁶⁹ The theory of lubrication was also discussed by MacConaill.¹²⁷⁰ One joint surface must be more curved than the other in order that synovial fluid may form a lubricating film which is wedge-shaped toward the region of contact. Fat pads reduced "mechanical curvature" and intra-articular discs increased it.

EXPERIMENTAL ARTHRITIS

The ability of various microorganisms and sensitizing agents to produce joint changes in experimental animals was further studied. Much interest again centered on the arthritis produced in rats by pleuropneumonia-like organisms. In a systematic series of studies, Tripi, Kuzell and associates determined the influence of a variety of drugs and other factors on the arthritis produced by an L, strain. The arthritis was prevented by aurothioglucose. 2000 Its incidence and severity were increased by corticotropin, BAL, thiouracil, pregnenolone, acetylsalicylic acid and glutathione, 628, 1152, 2070 but were not influenced by either cortisone or thyroidectomy. 1188, 2070 Exposure to cold or ultraviolet light increased the mortality from infection, but did not influence the joint involvement.2068 Aureomycin and terramycin prevented the development of arthritis, and salazopyrin lessened its incidence. 1158, 1154 Others found streptomycin effective in preventing arthritis and other manifestations of infection by pleuropneumonia-like organisms in rats. 1897 Arthritis in mice that was produced by the intravenous injection of Streptobacillus moniliformis was most effectively treated by streptomycin, although penicillin was also effective. 1200 [Effectiveness of various agents in the prevention and treatment of arthritis in rats due to pleuropneumonia-like organisms cannot be translated to the treatment of rheumatoid arthritis, as has at times been implied.—Ed.]

Findlay 540 summarized the characteristics and pathogenicity of pleuropneumonialike organisms recovered from various species, including man: certain strains "have a predilection for joint structures; they may cause an acute suppurative arthritis or a more chronic proliferative change." He concluded that efforts to incriminate these organisms in rheumatic fever and rheumatoid arthritis have failed, but that further investigation of their rôle in Haverhill fever (in association with Streptobacillus moniliformis) and in Reiter's syndrome appears worth while.

Arthritis was produced in rabbits by injecting a strain of enterococci isolated from the stools of patients with arthritis. Excessive use of the joints before inoculation increased the relative number of joints involved. The production of arthritis by living type I streptococci (isolated from a patient with scarlet fever) followed intravenous but not intracutaneous injection; acute phase protein and a rise in anti-

streptolysin titer followed either type of injection.832

Repeated intra-articular injection of typhoid somatic antigen resulted in an acute and chronic arthritis with synovial hypertrophy, focal accumulation of lymphocytes, and destruction of cartilage similar to changes observed in previous studies in which the same antigen had been injected intravenously. An intra-articular Schwartzman phenomenon, produced by injecting typhoid antigen into the joint and skin, with subsequent intravenous injection, resulted in vascular injury, hemorrhage, thrombosis and necrosis with continued active inflammation in the synovium for 27 days or longer. The presence of circulating antibodies at the time of the intra-articular injection of antigen did not alter its local effects. The intra-articular Arthus' reaction was also studied. 1879

The joint changes in experimental scurvy were carefully studied; characteristic features were intra-articular hemorrhage, subsynovial fibrous proliferation, and periarticular fibrosis, with little cartilage damage and no inflammation. In a large proportion of guinea pigs kept on diets partially deficient in vitamin C, the knees became stiff and painful. In this condition was attributed to edematous and degenerative changes in muscles and to the formation of hyperplastic connective tissue in and around the joint.

[The experimental production of arthritis by pituitary and adrenal hormones, and the influence of these hormones on experimental arthritis, are reviewed under the Adrenal Cortex and Rheumatic Diseases.—Ed.]

Spontaneous Arthritis in Animals

Diseases observed in swine were characterized by fever, myalgia, occasional subcutaneous nodules, skin rashes and arthritis, with varying degrees of limitation of joint motion. Postmortem examination revealed hypertrophy and increased vascularization of synovial villi with occasional pannus formation; pericardial adhesions and occasional pleuritic and peritoneal adhesions; often there was myocarditis, and occasionally vegetations on the heart valves. Many features were thought to resemble those of rheumatic or rheumatoid diseases. Administration of cortisone and ACTH led to definite improvement in three to four days, but relapses occurred two to 20 days after cessation of therapy.⁴⁵⁴

Outbreaks of polyarthritis in lambs followed inoculation with commercial sera that were later found to be contaminated with Erysipelothrix rhusiopathiae. The disease varied from an acute form with high fever and painful, swollen joints, to a more chronic form with gradually increasing loss of weight and strength, and increasing deformity of joints. Within three months, all animals inoculated with the contaminated sera had developed arthritis, and 25 per cent were dead; after

six months, all had died. In the early stage, postmortem examination of the joints showed excess fluid and "ulceration" of the cartilage. In chronic cases, the periarticular tissues were thickened by fibrous tissue formation, the synovial membranes were indurated, and there were vascular vegetative fringes at the borders of the cartilage. 485

THE CAMPAIGN AGAINST RHEUMATISM

From every county where data concerning both incidence and economic loss are reported, there is compelling evidence that arthritis is a major medical and social problem. There is a growing recognition by health authorities throughout the world that arthritis is the greatest single cause of protracted illness. In the United States at least 200,000 persons are totally and permanently disabled. 800,000 more are partially disabled, and 6,000,000 suffer in some degree from rheumatism or arthritis. 1771 The estimated yearly cost of medical care alone for the total number of patients with rheumatic disease in this country exceeds \$100,-In Canada, a survey made by the Dominion Bureau of Statistics in 1947 indicated that 22.6 per cent of an estimated 7,000,000 work-days lost because of illness was ascribed to arthritis or other rheumatic disease. 1642 In Switzerland, arthritis was listed as the cause of illness in 16.2 per cent of 93,750 reports of sickness among members of three national insurance organizations. Annual loss to the Swiss national economy as a result of arthritis was estimated at 40. 000,000 Swiss francs due to loss of work, 200,000,000 Swiss francs due to premature retirement, and 15,000,000 Swiss francs for cost of treatment. 184 Norgaard 1488 emphasized the social significance of chronic polyarthritis in the Scandinavian countries. In Denmark, data on Invalidity Insurance indicate that, of a population of about 4,000,000, one person each day becomes permanently disabled by this disease.

The serious concern of medical authorities and the general public over the economic waste due to rheumatism was reported from other countries. Lord Horder, who, with the Empire Rheumatism Council, has done so much to focus medical and public attention on this problem, estimated that there are 1,000,000 adult sufferers in England and Wales. BBB The financial cost in England was estimated to be £25,000,000 a year; to the National Health Insurance Fund alone

the cost was about £2,000,000 a year.⁸⁸⁵

The Scottish Department of Health in one year reported that the rheumatic group of diseases constituted the highest single cause of incapacity, accounting for 45,300 cases in an insured population of 1,837,000, and 3,000,000 days of incapacity. More than half of this time lost was for incapacities which lasted the whole year, a striking testimony to the crippling power of the disease.

The Ligue Internationale contre le Rheumatisme, with headquarters in Amsterdam, has as one of its important functions the spreading of information about rheumatic diseases throughout the world. The Ligue has encouraged the establishment of national committees in various countries, and this effort has proved so successful that in 1949 there were committees in 29 different countries. Under the auspices of the Ligue, the Seventh International Congress on Rheumatic Disease was held in New York City in 1949, permitting leading scientists in the field to exchange information and to hear at first hand the details of the

momentous discovery of the effect of cortisone and corticotropin on rheumatoid arthritis. A yearbook published by the *Ligue* in 1950 contains the rules, bylaws and lists of all members of the component societies throughout the world, and can be expected to stimulate collaboration and to facilitate the work of scientists of all countries in their struggle against one of the most distressing of human diseases. Largely through the efforts of the *Ligue* and its component national societies, the World Health Organization at the Fifth Assembly in June, 1952, approved the creation of an Expert Committee on Rheumatic Diseases.

The American Rheumatism Association, founded in 1930, includes among its 750 members most of the physicians in the United States and Canada who are especially interested in the rheumatic diseases. It has done much to keep the practicing physician in touch with current trends by means of two publications, the "Primer on the Rheumatic Diseases" and "Rheumatism Reviews." It has encouraged the formation of affiliated societies on a state, regional or city basis.

The American Rheumatism Association appreciated the need for public support and for funds to extend the attack on the rheumatic diseases. Shortly after World War II a committee was appointed to study the feasibility of a fundraising campaign. At about the same time three other independent groups in the United States launched fund-raising efforts. Through the able leadership of Dr. Paul Holbrook these separate fund-raising efforts were combined, and the Arthritis and Rheumatism Foundation was established on March 3, 1948. The professional and scientific policies of the Foundation are under the guidance of a committee nominated by the American Rheumatism Association, and thus the Association remains linked to the Foundation in an advisory capacity. Under the able leadership of Mr. Floyd Odlum a strong and active Board of Directors was formed, composed of influential laymen and representatives of the medical profession. 1846 The objectives of the Foundation are to organize an attack on the rheumatic diseases based upon research, specialized professional training, improved treatment facilities and public education. An intensive nation-wide campaign to make the public aware of the importance of rheumatic diseases has been launched, and a substantial start has been made in building the organization needed for an annual fund-raising effort. In less than five years the Foundation has established a network of 28 chapters in 30 states. During the Foundation's first three years a total of \$2,106,238 was raised. This means that the public is beginning to grasp the urgent need for a cooordinated attack on the rheumatic diseases.

The activities of the Foundation include financial support of basic and clinical research, establishment of clinical fellowships for the training of doctors, and aid for professional education in seminar courses, teaching conferences, and in the distribution to doctors of "The Bulletin on the Rheumatic Diseases." Also, to extend professional knowledge a color film, "Problems of Rheumatoid Arthritis" has been prepared and shown widely to medical and lay audiences. A pamphlet, "Arthritis and the Miracle Drugs," has been widely read by arthritic patients and their families. A comprehensive booklet on "Home Care in Rheumatoid Arthritis" has been prepared for distribution by physicians to their patients. Besides supporting a program of research fellowships in basic sciences related to rheumatic diseases, the Foundation functions through local city, state or regional Chapters. In addition to support of research projects, chapter activities have included provision of facilities for home

treatment by nurses trained in physical therapy, preparation annually of scientific papers on arthritis for a complete issue of each of the various journals of state medical societies, the awarding of grants to practitioners to study for three to six months in arthritis teaching centers, the sponsoring of round-table discussions for county medical societies, and the presentation of radio broadcasts on various aspects of the rheumatic diseases.

In 1949 the National Research Council undertook a survey designed to serve as a basis for the development of long-term research programs in arthritis and other rheumatic diseases. This survey revealed that only \$300,000 was being spent annually in the United States for research in the chronic rheumatic diseases. Neglect of hospital care for the arthritic patient was indicated by the disclosure that there were only 65 specially endowed beds for arthritic patients, as compared with 100,000 free beds available for tuberculous patients. It was estimated in this report that the yearly cost of medical care alone for the total number of rheumatic disease patients in this country exceeded \$100,000,000. After reviewing investigations of the rheumatic diseases which were in progress, this committee outlined under three main headings the need for specific research which should be undertaken; studies of connective tissue, of the disease processes,

and of their social and economic implications.

The introduction of ACTH and cortisone as research tools and as promising agents in the treatment of rheumatic diseases marked the beginning of a new era in the organized effort to combat this group of diseases. There was apparent an increased public demand for action and a move forward against arthritis.1771 In recognition of its serious concern about the widespread suffering caused by the rheumatic diseases, and in response to a growing public demand for expanded research to solve this problem, Congress on August 15, 1950, established a new Institute for Arthritis and Metabolic Diseases as one of the National Institutes of Health. An intensive program of research, aid to research and professional education in arthritis, rheumatism and allied metabolic diseases has been assured by this legislative act. Surgeon General Leonard A. Scheele,1771 in discussing the needs in this field, included the need for expanded research in hormonal compounds, particularly as tools for advancement of knowledge of normal man and his physiologic processes in health, the need for additional studies of the biologic and clinical effects of cortisone, ACTH and related new substances, the need for information regarding environmental, psychic and social factors in these diseases, and the need for development of ambulatory services, home-care programs and "Arthritis, rheumatism and related rehabilitation services for arthritic patients. ailments qualify as a public health problem."

In a review of the recent developments in the field of the rheumatic diseases, Waine 2100 pointed out that physiologic concepts have largely replaced the rigid descriptive approach to rheumatology and have fostered the definition of several rheumatic diseases in terms of systemic lesions. Another development has been the large-scale participation in rheumatologic research by physicians and scientists from other clinical and fundamental disciplines. This gain of additional workers experienced in the use of methods newly applied to the field has increased the rate and spread of research. To what extent the developments of recent years have brought us closer to the control and prevention of the rheu-

matic diseases remains for the future to tell.

BIBLIOGRAPHY

- Rheumatism Reviews: (a) First, Ann. Int. Med. 8: 1315, 1495, 1673, 1935. (b) Second, Ibid. 9: 883, 1936. (c) Third, Ibid. 10: 754, 1936. (d) Fourth, Ibid. 11: 1089, 1938. (e) Fifth, Ibid. 12: 1005, 1295, 1939. (f) Sixth, Ibid. 13: 1655, 1937, 1940. (g) Seventh, Ibid. 14: 1383, 1631, 1941. (h) Eighth, Ibid. 15: 1002, 1941. (i) Ninth, Ibid. 28: 66-168, 309-451, 1948.
- Abbasy, A. S. A.: Compression myelitis due to subperiosteal typhoid abscess, Arch. Pediat. 63: 63 (Feb.) 1946.
- Abel, M. S.: Sacroiliac joint changes in traumatic paraplegics, Radiology 55: 235 (Aug.) 1950.
- Abel, M. S., and Lomhoff, I. I.: The treatment of bursitis and peritendinitis calcarea
 of the shoulder joint by roentgen therapy, Permanente Found. M. Bull. 7: 90 (July)
 1949.
- Abrahams, A.: Rheumatic symptoms in general medicine, Practitioner 157: 131 (Aug.) 1946.
- Abrahams, D. G.: Q-T interval in acute rheumatic carditis, Brit. Heart J. 11: 342 (Oct.) 1949.
- Abrams, R., Hammarsten, E., and Shemin, D.: Glycine as a precursor of purines in yeast, J. Biol. Chem. 173: 429, 1948.
- Abramson, D. J., and Kamberg, S.: Spondylitis, pathological ossification, and calcification associated with spinal-cord injury, J. Bone and Joint Surg. 31A: 275 (Apr.) 1949.
- Adams, C. H., and Cecil, R. L.: Gold therapy in early rheumatoid arthritis, Ann. Int. Med. 33: 163 (July) 1950.
- Adams, F. H., and Dwan, P. F.: Cortisone and ACTH in rheumatic fever, Journal-Lancet 70: 389 (Oct.) 1950.
- Adams, J. C.: Prolapsed intervertebral disc with special reference to use and limitations of conservative treatment, M. Press 223: 543 (June) 1950.
- Adams, J. D., and Coonse, G. K.: Back injuries in industry, Am. J. Surg. 74: 258 (Sept.) 1947.
- Adamson, W. B.: Is orthodox therapy of rheumatic fever conducive to psychosomatic disability? Am. Heart J. 33: 715 (May) 1947.
- Adlersberg, D.: Newer advances in gout, Bull. New York Acad. Med. 25: 651 (Oct.) 1949.
- Adlersberg, D., Schaefer, L. E., and Drachman, S. R.: Development of hypercholesteremia during cortisone and ACTH therapy, J. A. M. A. 144: 909 (Nov.) 1950.
- Ahlberg, A.: Radical operative treatment of tuberculous hip; report of 113 cases, J. Bone and Joint Surg. 30A: 550 (July) 1948.
- Aikawa, J. K.: Hypersensitivity and rheumatic fever, Ann. Int. Med. 23: 969 (Dec.) 1945.
- Aisner, M., and Hoxie, T. B.: Bone and joint pain in leukemia, simulating acute rheumatic fever and subacute bacterial endocarditis, New England J. Med. 238: 733 (May) 1948.
- Aitken, A. P., and Bradford, C. H.: End results of ruptured intervertebral discs in industry, Am. J. Surg. 73: 365 (Mar.) 1947.
- 19. Aitken, D. M.: Legg-Perthes' disease, M. Press 218: 184 (Aug.) 1947.
- Aldred-Brown, G. R. P.: Early recognition of disease; non-specific arthritis in adults, Practitioner 157: 141 (Aug.) 1946.
- 20. Alexander, G. L.: Prolapsed intervertebral disc, Edinburgh M. J. 54: 14 (Jan.) 1947.
- Alexander, W. R. M., and Duthie, J. J. R.: Progesterone in the treatment of rheumatoid arthritis; a clinical trial in 5 cases, Lancet 1: 297 (Feb.) 1950.

- Alimurung, M. M., and Cruz, J. R.: Clinical observations on the value of Speransky treatment of spinal pumping in infectious arthritis, J. Philippine M. A. 23: 585 (Dec.) 1947.
- Allan, F. N., Lathrop, F. D., and Toumey, J. W.: Symposium on pain in head, neck and shoulder region, Lahey Clin. Bull. 5: 52 (Oct.) 1946.
- Allbritten, F. F., Jr., and Maltby, G. L.: Causalgia secondary to injury of major peripheral nerves: treatment by sympathectomy. Surgery 19: 407 (Mar.) 1946.
- Allen, J. C. B., and Shearman, C. H.: Traumatic radio-humeral synovitis, with pathological reports, M. J. Australia 1: 48 (Jan.) 1947.
- Allsop, J., and Smith, K. V.: Case of Schonlein-Henoch syndrome, M. J. Australia 2: 418 (Sept.) 1949.
- Alston, J. M., Cheng, K. K., and Short, R. H. D.: Unsuccessful attempts to produce periarteritis nodosa experimentally, J. Path. and Bact. 59: 490 (July) 1947.
- Altemeier, W. A., Snyder, H., and Howe, G.: Penicillin therapy in rat bite fever, J. A. M. A. 127: 270 (Feb.) 1945.
- Altman, K. I., Smull, K., and Barron, E. S. G.: A new method for the preparation of uricase and the effect of uricase on the blood uric acid levels of the chicken, Arch. Biochem. 21: 158 (Mar.) 1949.
- Altschule, M. D., Parkhurst, B. H., and Promisel, E.: Effects of intravenous injection of typhoid vaccine on blood leukocytes and adrenal cortex, Arch. Int. Med. 86: 505 (Oct.) 1950.
- Altshuler, C. H., and Angevine, D. M.: Histochemical studies on the pathogenesis of fibrinoid, Am. J. Path. 25: 1061 (Sept.) 1949.
- Anderson, A. B.: Anaphylactic purpura following intramuscular penicillin therapy, M. J. Australia 1: 305 (Mar.) 1947.
- Anderson, C. R.: Longitudinal grooving of nails caused by synovial lesions, Arch. Dermat. and Syph. 55: 828 (June) 1947.
- 34. Anderson, H. C., Kunkel, H. G., and McCarty, M.: Quantitative antistreptokinase studies in patients infected with group A hemolytic streptococci; comparison with serum antistreptolysin and gamma globulin levels with special reference to occurrence of rheumatic fever, J. Clin. Investigation 27: 425 (July) 1948.
- Anderson, H. C., and McCarty, M.: Determination of C-reactive protein in the blood as a measure of the activity of the disease process in acute rheumatic fever, Am. J. Med. 8: 445 (Apr.) 1950.
- Anderson, I. A.: Postmenopausal osteoporosis, clinical manifestations, and treatment with oestrogens, Quart. J. Med. 19: 67 (Jan.) 1950.
- Anderson, J. R.: Dysfunction of the temporomandibular joint, New Orleans M. and S. J. 103: 34 (July) 1950.
- Angel, J. L.: Skeletal change in ancient Greece, Am. J. Phys. Anthropol. 4: 69 (Mar.) 1946.
- 39. Angevine, D. M.: Pathology of rheumatic diseases, Radiology 49: 1 (July) 1947.
- 40. Anglin, A.: Sarcoidosis, Canad. M. A. J. 56: 177 (Feb.) 1947.
- Ant, M.: Treatment of myopathies and industrial injuries with wheat germ oil, Indust. Med. 15: 399 (June) 1946.
- 42. Ant, M.: Discussion of the papers, Ann. New York Acad. Sc. 52: 394 (Oct.) 1949.
- Ant, M., and Mamelok, A. E.: Vitamin E in the treatment of fibrositis with complicating osteoarthritis; case report, M. Times. New York 76: 162 (Apr.) 1948.
- Antopol, W.: Anatomic changes produced in mice treated with excessive doses of cortisone, Proc. Soc. Exper. Biol. and Med. 73: 262 (Feb.) 1950.
- 45. Apfelbach, G. L.: Bursitis, Indust. Med. 19: 476 (Oct.) 1950.
- Appelman, D. H., Feiman, M. S., and Harris, L.: Acute rheumatic fever in the aged, Am. Heart J. 37: 982 (May) 1949.
- 47. Archer, B. H.: Rheumatoid arthritis treated with massive doses of human chorionic

hormone to produce "pseudopregnancy," New York State J. Med. 50: 1265 (May) 1950.

- Arden, G. P., and Scott, J. C.: Lymph-gland biopsies for suspected bone and joint tuberculosis; analysis of 100 consecutive cases, Brit. M. J. 2: 87 (July) 1947.
- Arendshorst, W., and Falls, H. F.: Rôle of the adrenal cortex in treatment of ocular diseases with pyrogenic substances, Arch. Ophth. 44: 635 (Nov.) 1950.
- Arkin, A. M., and Schein, A. J.: Aseptic necrosis in Gaucher's disease, J. Bone and Joint Surg. 30A: 631 (July) 1948.
- Armour, G.: Rheumatoid arthritis; physiotherapy and psychotherapy in spa treatment, Brit. J. Phys. Med. 13: 19 (Jan.) 1950.
- 52. Armstrong, J. R.: Supraspinatus syndrome, Lancet 1: 94 (Jan.) 1947.
- Armstrong, J. R.: Orthopaedic treatment of painful shoulder, Rheumatism 5: 124 (Oct.) 1949.
- Arnold, H. L., Jr.: Systemic lupus erythematosus, Arch. Dermat. and Syph. 62: 632 (Nov.) 1950.
- Arnold, J. G., Jr.: The "sign of interlaminal tenderness," an important aid in the diagnosis and localization of intervertebral disc protrusions, Bull. School Med. Univ. Maryland 35: 145 (Oct.) 1950.
- Aronson, S. M., and Wallerstein, L.: Protean nature of scleroderma—with note on pulmonary changes, New York State J. Med. 50: 2723 (Nov.) 1950.
- Ash, R.: First ten years of rheumatic infection in childhood, Am. Heart J. 36: 89 (July) 1948.
- Ash, R.: Rheumatic infection in childhood: fifteen to twenty year follow-up: caution against early ambulant therapy, Am. J. Dis. Child. 76: 46 (July) 1948.
- Astbury, W. T.: Croonian lecture: On structure of biological fibres and problems of muscle, Proc. Roy. Soc., London, s.B 134: 303, 1947.
- Astrup, P., Brøchner-Mortensen, K., Faber, V., Hamburger, C., Harboe, N., Schmith, K., Snorrason, E., Sprechler, M., and Vesterdal, J.: The effects of adrenocorticotrophic hormone (ACTH) in a case of juvenile rheumatoid arthritis, Acta pædiat. 39: 215, 1950.
- Ayre, W. B.: Case of hypertrophic osteoarthropathy, Canad. M. A. J. 56: 71 (Jan.) 1947.
- Ayvazian, L. F., and Badger, T. L.: Disseminated lupus erythematosus occurring among . student nurses, New England J. Med. 239: 565 (Oct.) 1948.
- Babbitt, H. M.: Calcification of prepatellar bursa, J. M. Soc. New Jersey 47: 170 (Apr.) 1950.
- Bach, F.: Physical medicine and rheumatic diseases, Brit. J. Phys. Med. 10: 66 (May-June) 1947.
- Bach, F.: Non-articular rheumatism; "fibrositis," Brit. J. Phys. Med. 10: 132 (Sept.—Oct.) 1947.
- Bach, F.: Osteoarthritis of knee; notes on principles of Bisgaard in treatment, Brit. J. Phys. Med. 12: 124 (Sept.—Oct.) 1949.
- Bachman, A. L.: Roentgen diagnosis of knee-joint effusion, Radiology 46: 462 (May) 1946.
- Baehr, G., and Pollack, A. D.: Disseminated lupus erythematosus and diffuse scleroderma, J. A. M. A. 134: 1169 (Aug.) 1947.
- Baehr, G., and Soffer, L. J.: Treatment of disseminated lupus erythematosus with cortisone and adrenocorticotropin, Bull. New York Acad. Med. 26: 229 (Apr.) 1950.
- Baehr, G., Soffer, L. J., Boas, N. F., Levitt, M. F., and Gabrilove, J. L.: The influence of cortisone and adrenocorticotropin in disseminated lupus erythematosus, Tr. A. Am. Physicians 63: 89, 1950.
- Bailey, C. C., and Root, H. F.: Neuropathic foot lesions in diabetes mellitus, New England J. Med. 236: 397 (Mar.) 1947.

- Baines, G. H.: Relation of abacterial pyuria to Reiter's syndrome, Brit. M. J. 2: 605 (Oct.) 1947.
- Baker, A. H.: Lesion of the intervertebral disk caused by lumbar puncture, Brit. J. Surg. 34: 385 (Apr.) 1947.
- Baker, B. L., and Whitaker, W. L.: Interference with wound healing by local action of adrenocortical steroids, Endocrinology 46: 544 (June) 1950.
- Baker, D. M., and Chayen, M. S.: Treatment of arthritis by intra-articular injection, Lancet 1: 93 (Jan.) 1948.
- Baker, L. D.: Marie-Strümpell arthritis and the undiagnosed low back patient, Nebraska M. J. 33: 331 (Oct.) 1948.
- Baker, L. D., Coonrad, R. W., Reeves, R. J., and Hoyt, W. A., Jr.: Marie-Strümpell arthritis; follow-up study of roentgenographic, physical, and orthopaedic therapy, J. Bone and Joint Surg. 32A: 848 (Oct.) 1950.
- Baker, L. D., and Shutkin, N. M.: Peritendinitis of extensor pollicis brevis and abductor pollicis longus tendons—de Quervain's disease, North Carolina M. J. 8: 346 (June) 1947.
- Bakwin, H., and Lecks, H.: Meningococcemia without meningitis in children, M. Clin. North America 31: 581 (May) 1947.
- Balboni, V. G., Hollander, J. L., and Kydd, D. M.: Effect of prostigmine (neostigmine) on muscle spasm of rheumatoid arthritis, Am. J. M. Sc. 212: 153 (Aug.) 1946.
- Baldwin, J. S.: Follow-up study in rheumatic subjects previously treated with prophylactic sulfanilamide, J. Pediat. 30: 67 (Jan.) 1947.
- Baldwin, J. S.: Sulfadiazine prophylaxis in children and adolescents with inactive rheumatic fever, J. Pediat. 30: 284 (Mar.) 1947.
- Balensweig, I.: What can orthopedics offer the arthritic? M. Clin. North America 30: 635 (May) 1946.
- Ball, J.: Serum factor in rheumatoid arthritis agglutinating sensitized sheep red cells, Lancet 2: 520 (Nov.) 1950.
- Banyai, A. L., and Cadden, A. V.: Bacteriological examination of the gastric contents in the diagnosis and management of tuberculosis of the bones and joints, J. Bone and Joint Surg. 28: 137 (Jan.) 1946.
- Banyai, A. L., and Hirsh, L. H.: Acroerythrosis with associated analogous palmar changes in pulmonary tuberculosis, Urol. and Cutan. Rev. 50: 282 (May) 1946.
- 87. Barber, H. S.: Difficulties in diagnosis of rheumatic fever, Lancet 1: 122 (Jan.) 1946.
- 88. Bardhan, P. N.: Reiter's disease, Indian M. Gaz. 82: 577 (Oct.) 1947.
- Barford, L. J.: Sub-deltoid bursitis and a few other conditions causing pain in shoulder, Rheumatism 3: 12 (Apr.-June) 1946.
- Barnard, R. D., and Appel, A.: Scleroderma associated with malignant estrapenic leukoblastosis ("leukemia"); case report illustrating therapeutic response to orally administered crude "B₁₁" fermentation concentrates, Urol. and Cutan. Rev. 54: 345 (June) 1950.
- Barnes, A. R.: Effects of cortisone and ACTH in 14 patients with acute rheumatic fever, Proc. Staff Meet., Mayo Clin. 25: 478 (Aug.) 1950.
- Barnes, F. W., Jr., and Schoenheimer, R.: On biological synthesis of purines and pyrimidines, J. Biol. Chem. 151: 123 (Nov.) 1943.
- Barnes, G.: Investigation on rheumatic fever in Fiji, Tr. Roy. Soc. Trop. Med. and Hyg. 43: 413 (Jan.) 1950.
- Barnes, S. S., Moffatt, T. W., and Weiss, R. S.: Demonstration of L. E. cell in absence of anticoagulant, J. Invest. Dermat. 14: 397 (June) 1950.
- Barnes, S. S., Moffatt, T. W., Lane, C. W., and Weiss, R. S.: Studies on L. E. phenomenon, Arch. Dermat. and Syph. 62: 771 (Dec.) 1950.
- Barr, J. S.: Ruptured intervertebral disc and sciatic pain, J. Bone and Joint Surg. 29: 429 (Apr.) 1947.

97. Barsi, I.: New treatment of rheumatoid arthritis, Brit. M. J. 2: 252 (Aug.) 1947.

 Bartelink, D. L.: Myelography in intervertebral disk protrusion; horizontal beam examination with patient prone, Radiology 50: 202 (Feb.) 1948.

 Bartels, E. C.: Approach to diagnosis and treatment of gout, Bull. New England M. Center 9: 86 (Apr.) 1947.

 Bastow, J.: Orthopaedic aspects of rheumatoid arthritis, Ann. Rheumat. Dis. 5: 55 (Dec.) 1945.

101. Bastow, J.: Surgery of rheumatoid diseases, Post-Grad. M. J. 23: 325 (July) 1947.

102. Batchelor, J. S.: Excision of femoral head and neck for ankylosis and arthritis of hip, Post-Grad. M. J. 24: 241 (May) 1948.

103. Bauer, F. K., Riley, W. C., and Cohen, E. B.: Disseminated lupus erythematosus with Sydenham's chorea and rheumatic heart disease; report of case with autopsy, Ann. Int. Med. 33: 1042 (Oct.) 1950.

 Bauer, J. M., and Freyberg, R. H.: Vitamin D intoxication with metastatic calcification, J. A. M. A. 130: 1208 (Apr.) 1946.

 Bauer, J., and McDuffie, J. T.: Arthritic syndromes; Felty's syndrome and psoriatic polyarthritis in same patient, M. Rec. 159: 151 (Mar.) 1946.

 Bauer, W.: Rheumatoid arthritis: the importance of a comprehensive approach in treatment, J. A. M. A. 138: 397 (Oct.) 1948.

 Bauer, W.: Studies pertaining to articular structures and their disease, Mass. Gen. Hosp., The News, June-July 1950.

 Bauer, W., and Clark, W. S.: The systemic manifestations of rheumatoid arthritis, Tr. A. Am. Physicians 61: 339, 1948.

 Bauer, W., Giansiracusa, J. E., and Kulka, J. P.: The protean nature of the connective tissue diseases, Ann. Rheumat. Dis. 8: 309 (Dec.) 1949.

 Bauer, W., Giansiracusa, J. E., and Ropes, M. W.: The natural course of rheumatoid arthritis and the changes induced by ACTH, Tr. A. Am. Physicians 63: 76, 1950.

111. Baxter, C. R.: Reiter's disease, Brit. M. J. 2: 858 (Dec.) 1946.

 Baxter, H., Johnson, L., Mader, V., and Schiller, C.: Cortisone as an adjunct in the treatment of postoperative stiffness of the hand, Canad. M. A. J. 63: 540 (Dec.) 1950.

 Bayles, T. B.: Hypertrophic arthritis (degenerative joint disease), M. Clin. North America 34: 1435 (Sept.) 1950.

 Bayles, T. B., Judson, W. E., and Potter, T. A.: Reflex sympathetic dystrophy of the upper extremity (hand-shoulder syndrome), J. A. M. A. 144: 537 (Oct.) 1950.

 Bayles, T. B., Palmer, R. J., Massod, M. F., and Judd, E. H.: Vitamin B excretion studies in patients with rheumatoid arthritis, New England J. Med. 242: 249 (Feb.) 1950.

116. Bayles, T. B., Stout, C. F., Stillman, J. S., and Lever, W.: The treatment of scleroderma with adrenocorticotrophic hormone: preliminary observations, Proceedings of the first Clinical ACTH Conference, 1950, The Blakiston Company, Philadelphia, p. 447.

 Bean, E. O.: Osteochondritis and slipped femoral epiphysis, case report No. 145, Clin. Proc. Child. Hosp. 5: 107 (Mar.) 1949.

Becker, B. J. P.: Cardio-vascular disease in the Bantu and coloured races of South Africa; rheumatic heart disease, South African J. M. Sc. 11: 18 (Apr.) 1946.

 Beerman, H.: Visceral manifestations of scleroderma; review of recent literature, Am. J. M. Sc. 216: 458 (Oct.) 1948.

 Beerman, H., and Stokes, J. H.: The treatment of scleroderma, Am. J. M. Sc. 217: 453 (Apr.) 1949.

 Behrend, H. J.: Physical treatment of the "frozen shoulder," New York State J. Med. 48: 1035 (May) 1948.

Behrman, H. T., and Goodman, J. J.: Skin complications of cortisone and ACTH therapy, J. A. M. A. 144: 218 (Sept.) 1950.

- Bellach, H.: Dangers of artificial hyperpyrexia; report of a serious reaction from intravenous injection of typhoid vaccine, Connecticut M. J. 12: 813 (Sept.) 1948.
- Bellinger, D. H.: Present status of arthrosis of the temporomandibular joint, J. Oral Surg. 6: 9 (Jan.) 1948.
- Benditt, E. P., Schiller, S., Wong, H., and Dorfman, A.: Influence of ACTH and cortisone upon alteration in capillary permeability induced by hyaluronidase in rats, Proc. Soc. Exper. Biol. and Med. 75: 782, 1950.
- Benedict, J. D., Forsham, P. H., and Stetten, De W., Jr.: The metabolism of uric acid in the normal and gouty human studied with the aid of isotopic uric acid, J. Biol. Chem. 181: 183 (Nov.) 1949.
- 127. Benedict, J. D., Forsham, P. H., Roche, M., Soloway, S., and Stetten, DeW., Jr.: The effect of salicylates and adrenocorticotropic hormone upon the miscible pool of uric acid in gout, J. Clin. Investigation 29: 1104 (Aug.) 1950.
- 128. Bennett, G. A.: Malignant neoplasms originating in synovial tissues (synoviomata); study of 32 specimens registered at Army Institute of Pathology during war-time period, 1941-1945, J. Bone and Joint Surg. 29: 259 (Apr.) 1947.
- Bennett, G. A.: Reactive and neoplastic changes in synovial tissues (Richard Hermann Jaffe Memorial Lecture), Proc. Inst. Med. Chicago 18: 26 (Feb.) 1950.
- Bennett, G. A., and Paul, J. T.: Clinicopathologic conference, Am. J. Clin. Path. 19: 177 (Feb.) 1949.
- 131. Benning, N. M.: Chronic brucellosis; success of treatment with brucellin, J. A. M. A. 130: 320 (Feb.) 1946. Comment by M. J. Goodman, 131: 60 (May) 1946; reply by Benning, 131: 60 (May) 1946.
- 132. Bensley, E. H., Mitchell, S., and Wood, P.: Estimation of uric acid in serum and whole blood by electrophotometric modification of Folin's method, J. Lab. and Clin. Med. 32: 1382 (Nov.) 1947.
- Berg, C.: Orthopedic aspects of shoulder disabilities, Arch. Phys. Med. 31: 703 (Nov.) 1950.
- 134. Berg, R., Jr.: Arthralgia as first symptom of pulmonary lesions, Dis. of Chest 16: 483 (Oct.) 1949.
- 135. Bergman, B., and Kinberger, F. R.: A case report of the use of combined DOCA and ascorbic acid in a 12 year old child with rheumatoid arthritis, J. Pediat. 37: 774 (Nov.) 1950.
- Berliner, R. W., Hilton, J. G., Yü, T. F., and Kennedy, T. J., Jr.: The renal mechanism for urate excretion in man, J. Clin. Investigation 29: 396 (Apr.) 1950.
- Berman, L., Axelrod, A. R., Goodman, H. L., and McClaughry, R. I.: So-called "lupus erythematosus inclusion phenomenon" of bone marrow and blood; morphologic and serologic studies, Am. J. Clin. Path. 20: 403 (May) 1950.
- Berne, R. M.: An unusual sensitivity reaction to penicillin; report of a case with autopsy findings, New England J. Med. 242: 814 (May) 1950.
- Bernstein, L., and Broch, O. J.: Cardiac complications in spondylarthritis ankylopoietica, Acta med. Scandinav. 135: 185, 1949.
- 140. Bernstein, S. S.: Gout in early life, J. Mt. Sinai Hosp. 14: 747 (Sept.-Oct.) 1947.
- 141. Berry, J. V., and Berry, N. E.: Acute exudative cystitis of undetermined etiology, J. Urol. 58: 260 (Oct.) 1947.
- 142. Berthrong, M., Rich, A. R., and Griffith, P. C.: A study of the effect of adrenocortico-tropic hormone (ACTH) upon the experimental cardiovascular lesions produced by anaphylactic hypersensitivity, Bull. Johns Hopkins Hosp. 86: 131 (Mar.) 1950.
- Bertrand, J. J., Waine, H., and Tobias, C. A.: Distribution of gold in the animal body in relation to arthritis, J. Lab. and Clin. Med. 33: 1133 (Sept.) 1948.
- 144. Bettman, E. H., and Siffert, R. S.: Roentgen examination of the hip in Legg-Perthes' disease, Radiology 53: 548 (Oct.) 1949.

145. Bevans, M., and Taylor, H. K.: Lesion following the use of ertron in rheumatoid arthritis, Am. J. Path. 23: 367 (May) 1947.

 Bickel, W. H.: Osteoarthritis of the hip joint with special reference to treatment by cup arthroplasty, Am. J. Surg. 79: 420 (Mar.) 1950.

147. Bickel, W. H., Young, H. H., Pfuetze, K. H., and Norley, T.: Streptomycin in tuberculosis of bone and joint, J. A. M. A. 137: 682 (June) 1948.

148. Bidwell, E., van Heyningen, W. E., and Charlwood, B. A.: The biochemistry of the gas gangrene toxins. 5. The k-toxin (collagenase) of Clostridium welchii; addendum, electrophoresis of collagenase preparations, Biochem. J. 42: 140, 1948.

 Bien, E. J., and Troll, W.: Interference by glucose in the quantitative determination of uric acid, Proc. Soc. Exper. Biol. and Med. 73: 370, 1950.

 Bingham, C. T., Griffith, G. C., Solley, R. F., and Leake, W. H.: Problem of recurrence in rheumatic fever, U. S. Nav. M. Bull. 46: 367 (Mar.) 1946.

 Bingham, D. L. C.; Some industrial injuries of the shoulder joint, Canad. M. A. J. 61: 32 (July) 1949.

 Bingold, A. C., and Collins, D. H.: Hallux rigidus, J. Bone and Joint Surg. 32B: 214 (May) 1950.

153. Bishop, W. A., Jr.: Differential diagnosis of radiating pain from neck and shoulder girdle into the upper extremities, Arizona Med. 6: 25 (Mar.) 1949.

 Black, R. A.: Sanitarium care for the rheumatic child, Am. J. Occup. Therapy 1: 229 (Aug.) 1947.

 Blackburn, C. R.: Periarteritis nodosa simulating eosinophilic leukemia; case report, Am. J. M. Sc. 220: 313 (Sept.) 1950.

 Blackburn, C. R. B.: The role of lead in the reduction of the erythrocyte sedimentation rate by hyaluronidase, J. Biol. Chem. 178: 855 (Apr.) 1949.

 Blackman, N. S., and Hamilton, C. I., Jr.: Serial electrocardiographic changes in young adults with acute rheumatic fever; report of 62 cases, Ann. Int. Med. 29: 416 (Sept.) 1948.

Blanchard, K. C., Harvey, A. M., Howard, J. E., Kattus, A., Marshall, E. K., Jr., Newman, E. V., and Zubrod, C. G.: Effect of 3-hydroxy-2-phenylcinchoninic acid upon rheumatic fever, Bull. Johns Hopkins Hosp. 87: 50 (July) 1950.

159. Bland, E. F.: Rheumatic fever and rheumatic heart disease in North African and Mediterranean Theater of Operations, United States Army, Am. Heart J. 32: 545 (Nov.) 1946.

159a. Blazer, A., Friedman, H. H., and Steinbrocker, O.: Ineffectiveness of aluminum sub-acetate in rheumatoid arthritis, New England J. Med. 238: 507 (Apr.) 1948.

 Bleyer, L. F., and Carroll, K.: Villonodular plasma cell synovitis, Am. J. Surg. 74: 222 (Aug.) 1947.

 Block, W. D., and Geib, N. C.: Enzymatic method for determination of uric acid in whole blood, J. Biol. Chem. 168: 747 (May) 1947.

162. Block, W. D., Geib, N. C., and Robinson, W. D.: Metabolism, toxicity and manner of action of gold compounds in the treatment of arthritis; the effect of BAL and other thiol compounds in preventing the inhibition of oxygen consumption of rat tissues produced by gold salts, J. Lab. and Clin. Med. 33: 1381 (Nov.) 1948.

Bloom, J., and Rubin, J. H.: Transient pulmonary manifestations in rheumatoid arthritis, Canad. M. A. J. 63: 355 (Oct.) 1950.

 Bloom, W.: Pituitary implications in hypertrophic pulmonary osteoarthropathy, Ann. Int. Med. 29: 361 (Aug.) 1948.

165. Bloomfield, A. L.: Visceral angiitis, Stanford M. Bull. 4: 32 (Feb.) 1946.

166. Blunt, J. W., Jr., Plotz, C. M., Lattes, R., Howes, E. L., Meyer, K., and Ragan, C.: Effect of cortisone on experimental fractures in the rabbit, Proc. Soc. Exper. Biol. and Med. 73: 678 (Apr.) 1950.

- Bogdanovitch, A.: Neonatal arthritis due to Proteus vulgaris, Arch. Dis. Childhood 23: 65 (Mar.) 1948.
- Bograd, N., and Peters, G. S.: Scalenus anticus syndrome; consideration of diagnosis and treatment, J. M. A. Alabama 17: 361 (May) 1948.
- Bohan, P. T.: Concomitant diseases or conditions associated with polyarthritis, Postgrad. Med. 1: 384 (May) 1947.
- Bohatirchuk, F.: Multiple destructive processes of phalanges of hand with simultaneous calcifications of soft tissues of indefinite etiology, Am. J. Roentgenol. 64: 649 (Oct.) 1050.
- Boland, E. W.: Medical progress: rheumatoid spondylitis; its general features and management, California Med. 65: 285 (Dec.) 1946.
- 172. Boland, E. W.: Medical progress: rheumatoid arthritis; review of recent literature, California Med. 67: 315 (Nov.) 1947.
- 173. Boland, E. W.: Psychogenic rheumatism; the musculoskeletal expression of psychoneurosis, Ann. Rheumat. Dis. 6: 195 (Dec.) 1947; also, California Med. 68: 273 (Apr.) 1948.
- 174. Boland, E. W.: Recent advances in rheumatoid arthritis, California Med. 71: 362 (Nov.) 1949.
- 175. Boland, E. W.: The effects of cortisone and adrenocorticotropic hormone (ACTH) on certain rheumatic diseases, California Med. 72: 405 (June) 1950.
- Boland, E. W.: Relation of the adrenal cortex to rheumatic disease; a review of some recent investigations, Ann. Rheumat. Dis. 9: 1 (Mar.) 1950.
- Boland, E. W., and Headley, N. E.: Effects of cortisone acetate on rheumatoid arthritis, J. A. M. A. 141: 301 (Oct.) 1949.
- Boland, E. W., and Headley, N. E.: Management of rheumatoid arthritis with smaller (maintenance) doses of cortisone acetate, J. A. M. A. 144: 365 (Sept.) 1950.
- 179. Boland, E. W., and Headley, N. E.: Rheumatoid arthritis; clinical features and some of the current concepts in treatment, Ann. West. Med. and Surg. 2: 289 (July) 1948.
- Boland, E. W., and Headley, N. E.: Treatment of so-called palindromic rheumatism with gold compounds, Ann. Rheumat. Dis. 8: 64 (Mar.) 1949.
- Boland, E. W., Headley, N. E., and Hench, P. S.: The treatment of agranulocytosis with penicillin, J. A. M. A. 130: 556 (Mar.) 1946.
- Boland, E. W., Headley, N. E., and Hench, P. S.: The cerebrospinal fluid in rheumatoid spondylitis, Ann. Rheumat. Dis. 7: 195 (Dec.) 1948.
- Boland, E. W., and Shebesta, E. M.: Rheumatoid spondylitis; correlation of clinical and roentgenographic features, Radiology 47: 551 (Dec.) 1946.
- 184. Böni, A.: The problem of arthritis in Switzerland, Ann. Rheumat. Dis. 7: 175 (Sept.) 1948.
- Bonnin, J. G., and Boldero, J. L.: Air arthrography of the knee joint, Surg., Gynec. and Obst. 85: 64 (July) 1947.
- Bonsnes, R. W., and Dana, E. S.: On increased uric acid clearance following intravenous infusion of hypertonic glucose solutions, J. Clin. Investigation 25: 386 (May) 1946.
- Boots, R. H., and Ragan, C.: Rheumatic fever in adults simulating rheumatoid arthritis.
 Tr. A. Am. Physicians 62: 298, 1949.
- Boots, R. H., Coss, J. A., Jr., and Ragan, C.: Recent therapeutic experiences; gold sulfhydryl compounds, antireticular cytotoxic serum, and penicillin, Tr. A. Am. Physicians 60: 259, 1947.
- 189. Borden, A. L., Wallraff, E. B., Brodie, E. C., Holbrook, W. P., Hill, D. F., Stephens, C. A. L., Jr., Kent, L. J., and Kemmerer, A. R.: Plasma levels of free amino acids in normal subjects compared with patients with rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 75: 28 (Oct.) 1950.

 Bornstein, J., and Trewhella, P.: Adrenocorticotropic activity of blood-plasma extracts. Lancet 2: 678 (Dec.) 1950.

 Bosc, F. V. A.: Acid injections in the treatment of painful osteoarthritis, M. Press 220: 563 (Dec.) 1948.

 Bosworth, D. M., and Green, L. A.: Experiences with arthrodesis for tuberculosis of the hip, Quart. Bull., Sea View Hosp. 8: 39 (Jan.) 1946.

 Bosworth, D. M., Pietra, A. D., and Farrell, R. F.: Streptomycin in tuberculous bone and joint lesions with mixed infection and sinuses, J. Bone and Joint Surg. 32A: 103 (Jan.) 1950.

 Boucek, R. J., and Lowman, E. W.: A vascular approach to the treatment of rheumatoid arthritis; a preliminary report, Am. J. M. Sc. 215: 198 (Feb.) 1948.

 Bourne, W. A.: Sclerodactylia with oesophageal lesion (3 cases), Proc. Roy. Soc. Med. 40: 463 (June) 1947.

 Bowen, F. D. T.: Legg-Perthes' disease; report of 5 cases in adult men, Connecticut M. J. 10: 644 (Aug.) 1946.

 Bower, A. G., and Chudnoff, J. S.: Laboratory procedures in diagnosis of brucellosis. California Med. 69: 131 (Aug.) 1948.

 Bowers, R. E.: Histology of granuloma annulare compared with that of necrobiotic nodules of rheumatic arthritis, Brit. J. Dermat. 61: 247 (July) 1949.

 Bowes, J. H., and Kenten, R. H.: The amino-acid composition and titration curve of collagen, Biochem. J. 43: 358, 1948.

 Boyers, L. M.: Acute traumatic tenositis of the tendon calcaneus due to military boots. Mil. Surgeon 98: 500 (June) 1946.

 Bradfield, J. Y., and Hejtmancik, M. R.: Cardiac diseases and rheumatoid arthritis. Arch. Int. Med. 86: 1 (July) 1950.

 Bradford, F. K.: Lumbar intervertebral disc rupture, Dis. Nerv. System 11: 3 (Jan.) 1950.

203. Bradley, E. J.: Periarteritis nodosa in childhood, J. Pediat. 31: 78 (July) 1947.

 Brady, J. H., and Neal, W. S.: Splenectomy in case of disseminated lupus erythematosus with thrombocytopenic purpura, California Med. 68: 448 (June) 1948.

 Brailsford, J. F.: The radiology of bones and joints, 4th Ed., 1948, J. & A. Churchill. Ltd., London, p. 760.

 Brain, W. R., Knight, G. C., and Bull, J. W. D.: Discussion on rupture of intervertebral disc in cervical region, Proc. Roy. Soc. Med. 41: 509 (Aug.) 1948.

Branwood, A. W.: Clubbing of the fingers, Edinburgh M. J. 56: 105 (Mar.) 1949.
 Braude, A. I., Hall, W. H., and Spink, W. W.: Aureomycin therapy in human brucellosis due to *Brucella abortus*, J. A. M. A. 141: 831 (Nov.) 1949.

 Brenner, A. J.: Scleroderma with gastrointestinal involvement, Rev. Gastroenterol. 14: 869 (Dec.) 1947.

 Brenner, J. J., Leff, W. A., and Hochstein, E.: Lupus erythematosus disseminatus sine lupo with the nephrotic syndrome, Am. J. Med. 5: 288 (Aug.) 1948.

 Brentnall, E. S.: Diagnosis and treatment of tuberculosis of the hip joint in children. M. Press 222: 71 (July) 1949.

212. Brewer, T. F.: Rheumatic fever and rheumatic carditis treated with "pregnancy" hormones; a study of 97 cases over a 12 year period, 1938-1950, Connecticut M. J. 14: 489 (June) 1950.

 Brick, M., McKinley, H., Gourley, M., Roy, T. E., and Keith, J. D.: Oral penicillin prophylaxis in rheumatic fever patients, Canad. M. A. J. 63: 255 (Sept.) 1950.

 Brien, F. S.: Arthritis: its treatment in the home, Canad. M. A. J. 61: 583 (Dec.) 1949.

Briggs, H., and Keats, S.: Laminectomy and foraminotomy with chip fusions; operative treatment for relief of low-back pain and sciatic pain associated with spondylolisthesis, J. Bone and Joint Surg. 29: 328 (Apr.) 1947.

- Briggs, H., Keats, S., and Schlesinger, P. T.: Wedge osteotomy of spine with bilateral intervertebral foraminotomy; correction of flexion deformity in 5 cases of ankylosing arthritis of spine, J. Bone and Joint Surg. 29: 1075 (Oct.) 1947.
- Brinkman, G. L.: Arthritis complicating meningococcal meningitis, New Zealand M. J. 44: 327 (Dec.) 1945.
- Brixey, A. M., Jr., and Burke, R. M.: Arthro-onychodysplasia; hereditary syndrome involving deformity of head of radius, absence of patellas, posterior iliac spurs, dystrophy of finger nails, Am. J. Med. 8: 738 (June) 1950.
- 219. Brøchner-Mortensen, K., Georg, Joh., Hamburger, Chr., Snorrason, E., Sprechler, M., Videbaek, A. A., and With, T. K.: The effects of adrenocorticotrophic hormone (ACTH) in a case of chronic rheumatoid arthritis, Acta endocrinol. 3: 39, 1949.
- Brock, B. L.: Streptomycin in the treatment of tuberculous sinuses, Am. Rev. Tuberc.
 35 (July) 1948.
- 221. Brodie, E. C., Wallraff, E. B., Borden, A. L., Holbrook, W. P., Stephens, C. A. L., Jr., Hill, D. F., Kent, L. J., and Kemmerer, A. R.: Urinary excretion of certain amino acids during ACTH and cortisone treatment of rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 75: 285 (Oct.) 1950.
- 222. Brodsky, A. E.: Dermatomyositis, Bull. Hosp. Joint Dis. 10: 101 (Apr.) 1949.
- Brodsky, A. E.: Synovial osteochondromatosis of the shoulder, Bull. Hosp. Joint Dis. 11: 14 (Apr.) 1950.
- 224. Bronitsky, J.: Chondromalacia patellae, J. Bone and Joint Surg. 29: 931 (Oct.) 1947.
- Brown, A.: Ehlers-Danlos syndrome: description of 3 cases, Glasgow M. J. 27: 7 (Jan.) 1946.
- Brown, E. A.: Reactions to penicillin; a review of the literature, 1943-1948, Ann. Allergy 6: 723 (Nov.-Dec.) 1948.
- Brown, E. E.: Cause of cracking joints; relation to weather and fibrositis, Northwest Med. 48: 537 (Aug.) 1949.
- Brown, E. E.: Petechiae in children; incidence, seasonal variations, and etiology, J. Pediat. 32: 55 (Jan.) 1948.
- Brown, E. E., and Wasson, V. P.: Capillary fragility and menses in rheumatic girls, J. Pediat. 30: 455 (Apr.) 1947.
- Brown, E. M., Jr., Lukens, F. D. W., Elkinton, J. R., and DeMoor, P.: Observations
 on the metabolic and antiarthritic effects of ACTH and cortisone in diabetics, J.
 Clin. Endocrinol. 10: 1363 (Nov.) 1950.
- Brown, J., and Mallory, G. K.: Renal changes in gout, New England J. Med. 243: 325 (Aug.) 1950.
- 232. Brown, J. B., and Peterson, L. W.: Ankylosis and trismus resulting from war wounds involving the coronoid region of the mandible; report of 3 cases, J. Oral Surg. 4: 258 (July) 1946.
- Brown, R., Bunim, J. J., and McEwen, C.: Differential sheep-cell agglutination test in rheumatoid arthritis, Ann. Rheumat. Dis. 8: 299 (Dec.) 1949.
- 234. Brown, T. M., Wichelhausen, R. H., Robinson, L. B., and Merchant, W. R.: The in vivo action of aureomycin on pleuropneumonia-like organisms associated with various rheumatic diseases, J. Lab. and Clin. Med. 34: 1404 (Oct.) 1949.
- 235. Brown, T. McP., Wichelhausen, R. H., Merchant, W. R., and Robinson, L. B.: A study of the antigen-antibody mechanism in rheumatic diseases, Tr. Am. Clin. and Climatol. A. 62: 108, 1950.
- Browning, J. S., Rice, R. M., Lee, W. V., and Baker, L. M.: Gold therapy in rheumatoid arthritis, New England J. Med. 237: 428 (Sept.) 1947.
- Brownlee, G.: Effect of deoxycortone and ascorbic acid on formaldehyde-induced arthritis in normal and adrenalectomized rats, Lancet 1: 157 (Jan.) 1950.
- 238. Brudno, J. C.: Chronic relapsing febrile nodular nonsuppurative panniculitis (Weber-

Christian disease); relation to rheumatic fever and allied diseases, New England J. Med. 243: 513 (Oct.) 1950.

 Bruetsch, W. L.: Rheumatic brain disease; late sequel of rheumatic fever, J. A. M. A. 134: 450 (May) 1947.

 Brugsch, H. G., and Gill, D.: Polyarthritis in sickle-cell anemia, New England J. Med. 231: 291 (Aug.) 1944.

 Brunsting, L. A., Slocumb, C. H., and Didcoct, J. W.: Effects of cortisone on acute disseminated lupus erythematosus, Proc. Staff Meet., Mayo Clin. 25: 479 (Aug.) 1950.

 Brussell, I. J.: Temporomandibular joint diseases: differential diagnosis and treatment, J. Am. Dent. A. 39: 532 (Nov.) 1949.

243. Buchanan, J. M., Sonne, J. C., and Delluva, A. M.: Biologic precursors of uric acid; role of lactate glycine and carbon dioxide as precursors of carbon chain and nitrogen atom 7 of uric acid, J. Biol. Chem. 173: 81 (Mar.) 1948.

 Buchman, J., and Blair, J. E.: Precautionary administration of penicillin in surgical procedures on bones and joints, Arch. Surg. 55: 743 (Dec.) 1947.

Buckley, C. W.: Chronic rheumatic diseases from services in Emergency Medical Service hospitals, Ann. Rheumat. Dis. 5: 122 (June) 1946.

246. Buckley, C. W.: Osteoarthritis, Brit. M. J. 1: 1415 (June) 1950.

247. Bucy, P. C.: The simulation of multiple sclerosis and other degenerative diseases of the spinal cord by herniation of cervical intervertebral discs, Cincinnati J. Med. 30: 16 (Jan.) 1949.

Bulger, T. J.: Periarteritis nodosa; case requiring surgery, with review of literature.
 Delaware State M. J. 19: 59 (Apr.) 1947.

 Bunim, J. J.: Pneumococcic arthritis treated with penicillin; report of 6 cases, M. Clin. North America 30: 584 (May) 1946.

250. Bunim, J. J.: Infectious arthritides, Bull. U. S. Army M. Dept. 8: 458 (June) 1948.

 Bunnell, I. L., and Furcolow, M. L.: A report on ten proved cases of histoplasmosis. Pub. Health Rep. 63: 299 (Mar.) 1948.

 Burdick, W. F.: Still's disease (atrophic arthritis, atrophic rheumatoid arthritis or infectious rheumatoid arthritis), South. M. J. 39: 626 (Aug.) 1946.

253. Burgess, J. F., and Pritchard, J. E.: Tocopherols (vitamin E); treatment of lupus erythematosus; preliminary report, Arch. Dermat. and Syph. 57: 953 (June) 1948.

 Burks, J. W., Jr., and Thompson, P. E.: Coccidioidomycosis, South. M. J. 39: 613 (Aug.) 1946.

255. Burnet, J.: Comment on rheumatic pneumonitis, J. A. M. A. 134: 1042 (July) 1947.

Burrows, H. J.: Internal derangement of the knee, M. Press 218: 328 (Oct.) 1947.
 Burt, C. E., and Caplan, S. M.: Unusual reaction to penicillin in oil and wax, New England J. Med. 238: 804 (June) 1948.

 Burt, H. A.: Physical treatment in the rheumatic diseases and in some other painful condition, Brit. J. Phys. Med. 11: 173 (Nov.-Dec.) 1948.

Butts, D. C. A., and Olansky, S.: Observations on the cause and transmission of granuloma inguinale, Arch. Dermat. and Syph. 54: 524 (Nov.) 1946.

 Buxton, R., and Eickhoff, E. C.: Atrophic arthritis, splenomegaly and leukopenia; report of 2 cases, South. Med. and Surg. 111: 269 (Sept.) 1949.

Bywaters, E. G. L.: A variant of rheumatoid arthritis characterized by recurrent digital pad nodules and palmar fasciitis, closely resembling palindromic rheumatism, Ann. Rheumat. Dis. 8: 2 (Mar.) 1949.

262. Bywaters, E. G. L.: Discussion on the management of rheumatic fever and its early complications; general management of rheumatic fever, Proc. Roy. Soc. Med. 43: 199 (Mar.) 1950.

263. Bywaters, E. G. L.: Relation between heart and joint disease including "rheumatoid heart disease" and chronic post-rheumatic arthritis (type Jaccoud), Brit. Heart J. 12: 101 (Apr.) 1950.

- 264. Bywaters, E. G. L., Dixon, A. St. J., and Wild, J. B.: Deoxycortone and ascorbic acid in the treatment of rheumatoid arthritis, Lancet 1: 951 (May) 1950.
- Cahall, W. L.: Treatment of acute rheumatic fever, M. Clin. North America 30: 1332 (Nov.) 1946.
- Caldwell, G. A., and Unkauf, B. M.: Results of treatment of subacromial bursitis in 340 cases, Ann. Surg. 132: 432 (Sept.) 1950.
- 267. Calthrop, G. T.: X-ray diagnosis of gout, Rheumatism 3: 43 (Oct.-Dec.) 1946.
- Cameron, C., and Dawson, E. K.: Sarcoidosis-manifestation of tuberculosis, Edinburgh M. J. 53: 465 (Sept.) 1946.
- 269. Camiel, M. R.: Tuberculous arthritis of the shoulder, Radiology 46: 569 (June) 1946.
- Camp, J. D., and Scanlan, R. L.: Chronic idiopathic hypertrophic osteo-arthropathy, Radiology 50: 581 (May) 1948.
- Camp, P. D., and Calvin, L.: Severe and fatal rheumatic fever with pancarditis in Virginia, Virginia M. Monthly 74: 304 (July) 1947.
- 272. Campbell, A. M. G.: Ankylosing spondylitis; review of 25 cases, Lancet 1: 406 (Mar.)
- Campbell, E., and Whitfield, R. D.: Certain reasons for failure following disk operations, New York State J. Med. 47: 2569 (Dec.) 1947.
- 274. Capener, N.: Physiological rest, with special reference to arthritis and nerve lesions and to manufacture of appliances (Arris and Gale lecture, abstract), Brit. M. J. 2: 761 (Nov.) 1946.
- 275. Capener, N.: The clinical significance and treatment of lesions of the intervertebral disk, Ann. Rheumat. Dis. 8: 59 (Mar.) 1949.
- Caplan, P. S., and Margolis, H. M.; Reflex sympathetic dystrophy, Am. Pract. 2: 814 (Aug.) 1948.
- Carey, R. A., Harvey, A. M., and Howard, J. E.: Effect of adrenocorticotropic hormone (ACTH) and cortisone on the course of disseminated lupus erythematosus and periarteritis nodosa, Bull. Johns Hopkins Hosp. 87: 425 (Nov.) 1950.
- Carey, R. A., Harvey, A. M., Howard, J. E., and Wagley, P. F.: Effect of adrenocorticotropic hormone (ACTH) and cortisone on drug hypersensitivity reactions, Bull. Johns Hopkins Hosp. 87: 354 (Nov.) 1950.
- Carlstrom, B., and Lovgren, O.: Treatment of rheumatoid arthritis with adenosintriphosphoric acid (ATP), Ann. Rheumat. Dis. 8: 293 (Dec.) 1949.
- Carnesale, P. L., and Waisman, R. C.: A rare case of Bacillus pyocyancus (Pseudo-monas aeruginosa) pyoarthrosis, Surgery 27: 939 (June) 1950.
- Carney, P. W., Fitts, W. T., Jr., and Kirby, C. K.: Gunshot wounds of the major joints, J. Bone and Joint Surg. 28: 607 (July) 1946.
- 282. Carroll, I. N., and Mahru, M.: Shoulder-hand syndrome following coronary heart disease; report of case, Delaware State M. J. 22: 52 (Mar.) 1950.
- 283. Case, J. T.: Low back pain: the x-ray viewpoint, Indust. Med. 18: 13 (Jan.) 1949.
- 284. Cass, E. E.: Interstitial keratitis occurring in a case of Reiter's disease, Brit. J. Ophth. 33: 454 (July) 1949.
- Cassel, J. M., and Kanagy, J. R.: Studies on the purification of collagen, U. S. Dept. Comm. J. Research, Nat. Bureau Stand. 42: 557, 1949.
- Castellanos, A., and Galan, E.: Sarcoidosis (Besnier-Boeck-Schaumann's disease); report of case in child simulating Still's disease, Am. J. Dis. Child. 71: 513 (May)
- Castleman, L., and Mandelbaum, R. A.: Gold poisoning and disseminated lupus erythematosus, Am. Pract. and Digest Treat. 1: 561 (June) 1950.
- 288. Castor, C. W., and Baker, B. L.: Local action of adrenocortical steroids on epidermis and connective tissue of skin, Endocrinology 47: 234 (Oct.) 1950.
- 289. Cattell, L. M., Jr.: Diasone as an adjunct in the treatment of tuberculosis of bones and joints in children, J. Internat. Coll. Surgeons 12: 12 (Jan.-Feb.) 1949.

 Cave, E. F.: Symposium on specific methods of treatment; pain in neck and upper extremity, M. Clin. North America 34: 1323 (Sept.) 1950.

 Cave, E. F., and Rowe, C. R.: Patella; its importance in derangement of knee, J. Bone and Joint Surg. 32A: 542, 566 (July) 1950.

292. Cavelti, P. A.: Studies on pathogenesis of rheumatic fever; experimental production of autoantibodies to heart, skeletal muscle, and connective tissue, Arch. Path. 44: 1 (July) 1947; also, Arch. Path. 44: 13 (July) 1947.

Cavelti, P. A.: Pathogenesis of glomerulonephritis and rheumatic fever; in vivo activation of tissue antigens as a result of streptococcic infection and consecutive formation of autoantibodies, Arch. Path. 44: 119 (Aug.) 1947.

294. Caven, W. R.: Backache and fibrositis; medical point of view, Canad. M. A. J. 57: 37 (July) 1947.

 Cecil, R. L.: Problem of dosage in the administration of gold salts for rheumatoid arthritis, M. Clin. North America 30: 545 (May) 1946.

Cecil, R. L.: Differential diagnosis of subacute febrile arthritis, Postgrad. Med. 1: 308

 (Apr.) 1947.

Cecil, R. L.: Present day treatment of arthritis, Tr. and Stud., Coll. Physicians, Philadelphia 15: 7 (Apr.) 1947.

298. Cecil, R. L.: Psoriatic arthritis, Chicago M. Soc. Bull. 51: 747 (Mar.) 1949.

 Cecil, R. L., and deGara, P. F.: Agglutination reaction for hemolytic streptococci in rheumatoid arthritis; its significance in diagnosis and treatment, Am. J. M. Sc. 211: 472 (Apr.) 1946.

Cecil, R. L., and Kammerer, W. H.: The treatment and management of chronic arthritis, New York Med. 6: (Apr. 20) 1950.

 Chapchal, G.: Denervation of hip joint for osteoarthritis, Rheumatism 6: 63 (Apr.) 1950.

 Charr, R., and Swenson, P. C.: Clubbed fingers, Am. J. Roentgenol. 55: 325 (Mar.) 1946.

 Chatterjee, R. N.: Incidence of arthritis in smallpox, Indian M. Gaz. 85: 49 (Feb.) 1950.

 Cheng, K. K.: Observations on dye excretion through synovial membrane after lumbosacral sympathectomy and circulatory obstruction, Quart. J. Exper. Physiol. 35: 135 (June) 1949.

Chitwood, W. R.: The importance of recognizing post-infarctional shoulder-hand syndrome, New England J. Med. 243: 813 (Nov.) 1950.

 Christman, L. D., and Buehler, V. L.: Improved shoulder wheel, Physiotherapy Rev. 30: 327 (Aug.) 1950.

 Church, R. E., and Ellis, A. R. P.: Cystic pulmonary fibrosis in generalised scleroderma; report of 2 cases, Lancet 1: 392 (Mar.) 1950.

 Cincotti, J. J., Salzberg, A. M., Boone, E. W., and Kelley, J. B.: Posterior tuberculous sinuses of vertebral origin; wound revision and closure with streptomycin permitting early spinal fusion, New England J. Med. 241: 193 (Aug.) 1949.

 Clark, N. S.: Dermatomyositis in childhood; report of 4 cases, Arch. Dis. Childhood 21: 160 (Sept.) 1946.

 Clark, W. G.: Effect of adrenochrome on spreading action of hyaluronidase and "capillary permeability," Exper. Med. and Surg. 7: 78 (May-Aug.) 1949.

 Clark, W. S.: The treatment of rheumatoid arthritis, M. Clin. North America 33: 1375 (Sept.) 1949.

312. Clarke, O.: Arthritis mutilans associated with psoriasis, Lancet 1: 249 (Feb.) 1950.

 Clawson, B. J., Noble, J. F., and Lufkin, N. H.: Nodular inflammatory and degenera tive lesions of muscles from 450 autopsies, Arch. Path. 43: 579 (June) 1947.

314. Clemmesen, S.: Rheumatic fever statistics in Denmark from 1878 to 1946 and their significance in profylaxis, Acta med. Scandinav., supp. 234: 109, 1949.

- Cleveland, M.: The emergency treatment of bone and joint casualties, J. Bone and Joint Surg. 32A: 235, 279 (Apr.) 1950.
- 316. (Clinical Conference) Histoplasmosis, J. Pediat. 31: 98 (July) 1947.
- 317. Combined Clinic: Rheumatoid arthritis, Am. J. Med. 1: 675, 1946.
- Clinico-Pathological Conference: Purpura, arthritis, hepatomegaly and hepatic failure, Am. J. Med. 1: 551 (Nov.) 1946.
- 319. Cloyd, A. D.: Diseases simulating arthritis, Nebraska M. J. 31: 194 (May) 1946.
- Co Tui, Kuo, N. H., and Simuangco, S.: Protein studies in scleroderma, J. Invest. Dermat. 15: 181 (Sept.) 1950.
- 321. Cobb, S., and Miles, H. H. W.: Psychiatric conference. Case report, Am. Pract. 3: 407 (Mar.) 1949.
- Coburn, A. F.: Rheumatic fever problem; present status (Benjamin Knox Rachford lecture), Am. J. Dis. Child. 70: 339 (Nov.-Dec.) 1945.
- Coburn, A. F.: Problems in prevention of rheumatic fever by reinforced diet, J. Am. Dietet. A. 26: 345 (May) 1950.
- 324. Code, C. F., Williams, M. M. D., Baldes, E. J., and Ghormley, R. K.: Are intervertebral disks displaced during positive acceleration? J. Aviation Med. 18: 231 (June) 1947.
- 325. Coggeshall, H. C.: Acute rheumatic fever in young adults, Texas State J. Med. 42: 430 (Nov.) 1946.
- 326. Cohen, A.: Gout in Negro family, Am. J. Med. 4: 911 (June) 1948.
- Cohen, A., Dubbs, A. W., and Goldman, J.: Rheumatoid arthritis; 475 cases treated with 721 courses of gold, Pennsylvania M. J. 52: 35 (Oct.) 1948.
- Cohen, A., Goldman, J., and Dubbs, A. W.: Treatment of acute gold and arsenic poisoning; use of BAL (2,3-dimercaptopropanol, British Anti-Lewisite), J. A. M. A. 133: 749 (Mar.) 1947.
- Cohen, A., Reinhold, J. G., and Cohn, R.: Metastatic calcification; is the role of hypercalcemia overemphasized as a toxic manifestation of vitamin D therapy in rheumatoid arthritis? Indust. Med. 17: 442 (Nov.) 1948.
- Cohen, A., Trommer, P., and Goldman, J.: Physostigmine for muscle spasm in rheumatoid arthritis, J. A. M. A. 130: 265 (Feb.) 1946.
- Cohen, A. E., and Kaufman, J.: The use of procaine hydrochloride intravenously in the treatment of reactions to penicillin; report of 4 cases, J. Allergy 19: 68 (Jan.) 1048
- Cohen, E. B.: Brucellosis at the State of Wisconsin General Hospital, Wisconsin M. J. 45: 847 (Sept.) 1946.
- Cohen, H.: Samuel Hyde memorial lecture: Rheumatic diseases; challenge and opportunity, Proc. Roy. Soc. Med. 40: 443 (June) 1947.
- 334. Coke, H.: Practical hypothesis for chrysotherapy, Rheumatism 3: 126 (Oct.) 1947.
- Collins, D. H.: Laboratory aids in the diagnosis of rheumatism, Practitioner 161: 180 (Sept.) 1948.
- Committee of American Rheumatism Association: Primer on the rheumatic diseases,
 J. A. M. A. 139: 1068 (Apr.) 1949.
- Conferences on therapy from Cornell University Medical College and New York Hospital; treatment of rheumatic fever, Am. J. Med. 2: 86 (Jan.) 1947.
- 338. Conn, J. W., and Louis, L. H.: Production of endogenous "salt-active" corticoids as reflected in the concentrations of sodium and chloride of thermal sweat, J. Clin. Endocrinol. 10: 12 (Jan.) 1950.
- 339. Conn, J. W., Louis, L. H., and Johnston, M. W.: Metabolism of uric acid, glutathione and nitrogen, and excretion of 11-oxysteroids and 17-ketosteroids during induction of diabetes in man with pituitary adrenocorticotropic hormone, J. Lab. and Clin. Med. 34: 255 (Feb.) 1949.
- 340. Conn, J. W., Louis, L. H., and Wheeler, C. E.: Production of temporary diabetes mel-

litus in man with pituitary adrenocorticotropic hormone; relation to uric acid metabolism, J. Lab. and Clin. Med. 33: 651 (June) 1948.

- Conner, S. K.: Climate and rheumatoid arthritis, Arizona Med. (no. 4) 4: 37 (July) 1947.
- Connor, C. A. R.: Experiences with rheumatic fever in Army Air Forces, Am. J. Pub. Health 36: 236 (Mar.) 1946.
- Coodley, E. L., and Greco, A. J.: Clinical aspects of ochronosis, Am. J. Med. 8: 816 (June) 1950.
- Coodley, E. L., Weiss, B. J., and Egeberg, R. O.: Reiter's syndrome; report of 6 cases, Ann. West. Med. and Surg. 2: 500 (Nov.) 1948.
- Copeman, W. S. C.: Rheumatism as a social and industrial problem, Brit. J. Phys. Med. 9: 66 (May-June) 1946.
- Copeman, W. S. C.: Chronic rheumatic diseases in World War 1939–1945, Ann. Rheumat. Dis. 5: 115 (June) 1946.
- Copeman, W. S. C.: The rheumatic diseases in the eighteenth century, West London Hosp., Dept. Rheumat. Dis., annual report, 1948.
- Copeman, W. S. C.: Fibro-fatty tissue and its relation to certain "rheumatic syndromes," Brit. M. J. 2: 191 (July) 1949.
- Copeman, W. S. C., and Ackerman, W. L.: Edema or herniations of fat lobules as cause of lumbar and gluteal "fibrositis," Arch. Int. Med. 79: 22 (Jan.) 1947.
- Copeman, W. S. C., Ellman, P., and Kersley, G. D.: Aetiology of chronic rheumatism, Proc. Roy. Soc. Med. 40: 329 (Apr.) 1947.
- Copeman, W. S. C., and Pugh, L. G. C.: Dehydration treatment of rheumatic fever, Lancet 2: 673 (Dec.) 1950.
- 352. Copeman, W. S. C., Savage, O., Bishop, P. M. F., Dodds, E. C., Gottlieb, B., Glyn, J. H. H., and Kellie, A. E.: A study of cortisone and other steroids in rheumatoid arthritis, Brit M. J. 2: 849 (Oct.) 1950.
- Cordes, F. C., and Aiken, S. D.: Ocular changes in acute disseminated lupus erythematosus; report of a case with microscopic findings, Am. J. Ophth. 30: 1541 (Dec.) 1047
- 354. Cormia, F. E., and Lewis, G. M.: Experimental aspects of penicillin sensitization, with special reference to conjoint sensitization to superficial fungous disease, J. Invest. Dermat. 7: 375 (Dec.) 1946.
- Cornbleet, T., Reed, C. I., and Reed, B. P.: X-ray diffraction studies in calcinosis, J. Invest. Dermat. 13: 171 (Oct.) 1949.
- Cortes, C., and Villarreal, H.: Clinical features of 1,160 cases of rheumatic valvular endocarditis, Am. Heart J. 33: 715 (May) 1947.
- Coss, J. A., Jr., Bauman, E., Boots, R. H., and Lipman, M. O.: Prolonged administration of penicillin in arthritis, Am. J. Med. 4: 710 (May) 1948.
- Coss, J. A., Jr., and Boots, R. H.: Juvenile rheumatoid arthritis; study of 56 cases with note on skeletal changes, J. Pediat. 29: 143 (Aug.) 1946.
- Costero, I.: Cerebral lesions responsible for death of patients with active rheumatic fever, Arch. Neurol. and Psychiat. 62: 48 (July) 1949.
- Coutts, W. E.: Testicle and spermatic tract lesions in lymphogranuloma venereum, Nature, London 158: 487 (Oct.) 1946.
- 362. Coventry, M. B.: Internal derangement of the knee, Minnesota Med. 30: 42 (Jan.) 1947.
- 363. Cowan, I. C., and Harkness, J.: Plasma viscosity in rheumatic diseases, Brit. M. J. 2: 686 (Nov.) 1947.
- Craig, N. S.: Epidemic myalgia-Bornholm disease, Bristol Med.-Chir. J. 67: 50 (Apr.) 1950.
- Craige, E., Alimurung, M. M., Bland, E. F., and Massell, B. F.: Q-T interval in rheumatic fever, Circulation 1: 1338 (June) 1950.

- 366. Crain, D. C.; Epidemic tropical arthritis, Ann. Rheumat. Dis. 6: 76 (June) 1947.
- Crain, D. C.: Rheumatoid arthritis of the spine, Bull. U. S. Army M. Dept. 9: 1005 (Dec.) 1949.
- Crain, D. C., Kyle, L. H., and Rubin, M.: The modern treatment of rheumatoid arthritis, Postgrad. Med. 8: 228 (Sept.) 1950.
- Cranfield, H. V.: Some limitations in use of occupational therapy, Occup. Therapy 26: 308 (Oct.) 1947.
- Crawford, A. S., Mitchell, C. L., and Granger, G. R.: Surgical treatment of low back pain with sciatic radiation; preliminary report on 346 cases, Arch. Surg. 59: 724 (Sept.) 1949.
- Crawford, G. N. C.: Experimental study of tendon growth in rabbit, J. Bone and Joint Surg. 32B: 234 (May) 1950.
- Creecy, A. A., and Beazlie, F. S., Jr.: Reiter's syndrome and focal infection, J. Urol. 59: 234 (Feb.) 1948.
- 373. Criep, L. H.: Allergy of joints, J. Bone and Joint Surg. 28: 276 (Apr.) 1946.
- 374. Crissey, R. E., and Day, A. J.: Ochronosis; case report, J. Bone and Joint Surg. 32A: 688 (July) 1950.
- Cruickshank, C. N., and Harrison, S. H.: Acute suppurative tenosynovitis treated with systemic penicillin, Lancet 2: 606 (Oct.) 1947.
- Curr, J. F.: Synovial osteochondromatosis; 2 uncommon examples, Brit. M. J. 2: 1020 (Nov.) 1949.
- 377. Currence, J. D.: Hydrotherapy in osteoarthritis, Ann. Int. Med. 32: 682 (Apr.) 1950.
- Currie, J. P., and Will, G.: Treatment of rheumatoid arthritis with deoxycortone and vitamin C, Lancet 1: 708 (Apr.) 1950.
- Curtis, A. C., and Grekin, R. H.: Sarcoidosis. III. A review, M. Clin. North America 33: 31 (Jan.) 1949.
- Curtis, A. C., and Horne, S. F.: Disseminated lupus erythematosus with pericardial effusion, Ann. Int. Med. 30: 209 (Jan.) 1949.
- Curtis, A. C., Taylor, H., Jr., and Grekin, R. H.: Sarcoidosis; results of treatment with varying amounts of calciferol and dihydrotachysterol, J. Invest. Dermat. 9: 131 (Sept.) 1947.
- 382. Cyriax, J.: Fibrositis, Brit. M. J. 2: 251 (July) 1948.
- Dahlberg, G., and Sundelin, F.: Rheumatoid arthritis and function of joints, Acta med. Scandinav. 135: 40, 1949.
- Dale, M.: Treatment of osteoarthritis with ACTH, J. Michigan M. Soc. 49: 1068 (Sept.) 1950.
- 385. Daley, A.: Chronic rheumatism, Rheumatism 4: 199 (July) 1948.
- 386. Darley, W.: Gold therapy in rheumatoid arthritis, Northwest Med. 46: 34 (Jan.) 1947.
- Darley, W.: Denver rheumatic fever diagnostic service. Purpose and method of operation, Pub. Health Rep. 64: 1631 (Dec.) 1949.
- Darley, W., and Gordon, R. W.: Brucella sensitization; clinical evaluation, Ann. Int. Med. 26: 528 (Apr.) 1947.
- Daugherty, G. W., and Baggenstoss, A. H.: Syndrome characterized by glomerulonephritis and arthritis; Libman-Sacks disease with predominantly renal involvement. Arch. Int. Med. 85: 900 (June) 1950.
- Davidson, L. S. P.: Physiological and clinical effects of cortisone and adrenocorticotrophic hormone (ACTH); Honyman Gillespie lecture, Edinburgh M. J. 57: 317 (Aug.) 1950.
- 391. Davidson, L. S. P., Duthie, J. J. R., and Sugar, M.: Focal infection in rheumatoid arthritis; comparison of incidence of foci of infections in upper respiratory tract in 100 cases of rheumatoid arthritis and 100 controls, Ann. Rheumat. Dis. 8: 205 (Sept.) 1949.

- Davies, D. V.: Anatomy and physiology of diarthrodial joints, Ann. Rheumat. Dis. 5: 29 (Dec.) 1945.
- 393. Davies, D. V.: Lymphatics of synovial membrane, J. Anat. 80: 21 (Jan.) 1946.
- Davies, D. V.: Synovial membrane and synovial fluid of joints (Arris and Gale lecture), Lancet 2: 815 (Dec.) 1946.
- 395. Davies, D. V.: The structure and functions of the synovial membrane, Brit. M. J. 1: 92 (Jan.) 1950.
- Davies, D. V., and Edwards, D. A. W.: The blood supply of the synovial membrane and intra-articular structures, Ann. Roy. Coll. Surgeons, England 2: 142 (Mar.) 1948.
- Davies, W.: Keratoderma blennorrhagica following Reiter's disease; report of a case successfully treated with massive doses of penicillin, Brit. J. Ven. Dis. 25: 155 (Sept.) 1949.
- Davis, D., and Ritvo, M.: Osteoarthritis of cervicodorsal spine (radiculitis) simulating coronary-artery disease; clinical and roentgenologic findings, New England J. Med. 238: 857 (June) 1948.
- 399. Davis, E.: Hereditary clubbing of digits in 2 families, Brit. M. J. 1: 128 (Jan.) 1946.
- Davis, J. B., and Blair, H. C.: Marie-Strümpell disease; report of 15 cases, J. Bone and Joint Surg. 32A: 838 (Oct.) 1950.
- Davis, N.: Symptomatology and diagnosis of chronic brucellosis, J. Indiana M. A. 39: 485 (Oct.) 1946.
- 401a. Davis, R. H.: Streptomycin in the treatment of tuberculous sinuses; review of 11 cases, Lancet 2: 982 (Nov.) 1949.
- Davison, R.: BAL therapy of dermatitis caused by injections of gold salts, Stanford M. Bull. 5: 37 (Feb.) 1947.
- Davison, R. A.: Painful shoulder and other neurotrophic disturbances of upper extremities caused by osteoarthritis of cervical spine, Stanford M. Bull. 5: 160 (Aug.) 1947.
- 403a. Davison, R. A., Koets, P., and Kuzell, W. C.: Effect of roentgenotherapy on urinary 17-ketosteroid excretion in ankylosing spondylarthritis, J. Clin. Endocrinol. 9: 79 (Jan.) 1949.
- Davison, R. A., Koets, P., and Kuzell, W. C.: Excretion of 17-ketosteroids in ankylosing spondylarthritis and in rheumatoid arthritis; preliminary report, J. Clin. Endocrinol. 7: 201 (Mar.) 1947.
- Davison, R., Koets, P., Snow, W. G., and Gabrielson, L. G.: Effects of delta 5-pregnenolone in rheumatoid arthritis, Arch. Int. Med. 85: 365 (Mar.) 1950.
- Davson, J., Ball, J., and Platt, R.: Kidney in periarteritis nodosa, Quart. J. Med. 17: 175 (July) 1948.
- Dawson, J. E., and Salt, H. B.: Erythrocyte sedimentation and plasma viscosity tests in rheumatic patients undergoing spa treatment, Brit. J. Phys. Med. 13: 152 (July) 1950.
- Day, T. D.: Connective tissue permeability and the mode of action of hyaluronidase, Nature, London 166: 785 (Nov.) 1950.
- Deaver, G. G., and Peterson, K. J.: Pulley exercises to increase joint movement, Arch. Phys. Med. 27: 17 (Jan.) 1946.
- 410. Debono, J. E.: Aureomycin in undulant fever, Lancet 2: 326 (Aug.) 1949.
- 411. Deery, E. M.: Laminectomy for Pott's paraplegia, Ann. Surg. 124: 201 (Aug.) 1946.
- 412. deGara, P. F.: Immunologic and biochemical studies in infants and children, with special reference to rheumatic fever; occurrence of agglutinins in normal and abnormal conditions, Pediatrics 2: 410 (Oct.) 1948.
- 413. Delafield, R. H.: Scalenus anticus syndrome, Am. Praçt. 3: 730 (Aug.) 1949.
- 414. Delano, P. J.: Pathogenesis of Charcot's joint, Am. J. Roentgenol. 56: 189 (Aug.) 1946.

- Dennie, C. C., and Morgan, D. B.: Treatment of certain types of scleroderma, South. M. J. 40: 860 (Oct.) 1947.
- Dennison, A. D., Jr.: Cardiologic aspects of certain rheumatic diseases, J. M. Soc. New Jersey 47: 4 (Jan.) 1950.
- Denny, E. R.: On current concepts of etiology and pathogenesis of periarteritis nodosa,
 J. Oklahoma M. A. 40: 220 (June) 1947.
- Denny, F. W., Wannamaker, L. W., Brink, W. R., Rammelkamp, C. H., Jr., and Custer, E. A.: Prevention of rheumatic fever; treatment of the preceding streptococcic infection. J. A. M. A. 143: 151 (May) 1950.
- DePalma, A. F.: Calcareous deposits in soft tissues about proximal interphalangeal joint of index finger; report of case, J. Bone and Joint Surg. 29: 808 (July) 1947.
- DePalma, A. F.: Scalenus anticus syndrome treated by surgery and skeletal traction, Am. J. Surg. 76: 274 (Sept.) 1948.
- Desmarais, M. H. L.: Rehabilitation of chronic arthritic, Brit. J. Phys. Med. 10: 116 (July-Aug.) 1947.
- Desmarais, M. H. L.: The phosphatase activity in spondylitis ankylopoietica, Ann. Rheumat. Dis. 7: 105 (June) 1948.
- Desmarais, M. H. L.: The neutral 17-ketosteroids in rheumatoid arthritis and spondylitis, Ann. Rheumat. Dis. 8: 296 (Dec.) 1949.
- Desmarais, M. H. L., Gibson, H. J., and Kersley, G. D.: Muscle histology in rheumatic and control cases; a study of 119 biopsy specimens, Ann. Rheumat. Dis. 7: 132 (Sept.) 1948.
- Diaz-Rivera, R. S., and Miller, A. J.: Periarteritis nodosa; clinicopathological analysis of 7 cases, Ann. Int. Med. 24: 420 (Mar.) 1946.
- Dickson, D. D., and Luckey, C. A.: Tenosynovitis of the extensor carpi ulnaris tendon sheath, J. Bone and Joint Surg. 30A: 903 (Oct.) 1948.
- 427. Dickson, F.: Industrial injuries of back, Occup. Med. 3: 53 (Jan.) 1947.
- Dickson, J. A., and Willien, L. J.: Arthrodesis of hip joint in degenerative arthritis; modified one-stage procedure with internal fixation, J. Bone and Joint Surg. 29: 687 (July) 1947; also, Rheumatism 3: 131 (Oct.) 1947.
- Dickson, W.: Some physiological aspects of fatigue fibrositis and arthritis, Tr. M. Soc. London (1940-1943) 63: 335, 1945.
- Dienes, L., Ropes, M. W., Smith, W. E., Madoff, S., and Bauer, W.: The role of pleuropneumonia-like organisms in genitourinary and joint diseases, New England J. Med. 238: 509, 563 (Apr.) 1948.
- Dienes, L., and Weinberger, H. J.: Pleuropneumonia-like organisms and their possible relation to articular disease, Ann. Rheumat. Dis. 8: 311, 1949.
- Dingman, R. O.: Ankylosis of the temporomandibular joint, Am. J. Orthodontics (Oral Surg. Sect.) 32: 120 (Feb.) 1946.
- 433. Dittrich, R. J.: Osteochondromatosis of elbow, Am. J. Surg. 72: 125 (July) 1946.
- Dittrich, R. J.: Subfascial fat abnormalities and low back pain, Minnesota Med. 33: 593 (June) 1950.
- Dobson, J.: Arthrodesis in tuberculosis of the hip joint; analysis of 50 cases, J. Bone and Joint Surg. 30B: 95 (Feb.) 1948.
- Dodds, J. C.: Treatment of sulfonamide-resistant gonorrhea with penicillin as clinic routine, J. Michigan M. Soc. 44: 1204 (Nov.) 1945.
- Dodge, H. J.: Rheumatic fever in Kootenai County, Idaho, Northwest Med. 48: 550 (Aug.) 1949.
- 438. Dole, V. P., and Rothbard, S.: Electrophoretic changes in the serum of a patient with rheumatoid arthritis, J. Clin. Investigation 26: 87 (Jan.) 1947.
- Donald, J. M.: Scalenus anticus and cervical rib syndrome, Texas State J. Med. 43: 495 (Dec.) 1947.

- Doolan, P. D., Cobey, M. C., and Kyle, L. H.: Adrenocorticotropic hormone therapy as adjunct to surgery in chronic tophaceous gout, South. M. J. 43: 780 (Sept.) 1950.
- Dordick, J. R., and Wasserman, M. M.: The differential sheep cell agglutination test in arthritis. Am. J. Clin. Path. 20: 526 (June) 1950.
- Dorfman, A., and Moses, F. E.: Effect of adrenocorticotrophic hormone (ACTH) on serum hyaluronidase inhibitor in rheumatic fever, Proc. Soc. Exper. Biol. and Med. 73: 667 (Apr.) 1950.
- Dorfman, A., Ott, M. L., and Whitney, R.: Hyaluronidase inhibitor of human blood, J. Biol. Chem. 174: 621 (June) 1948.
- 444. Dorfman, A., Reimers, E. J., and Ott, M. L.: Action of sodium salicylate on hyaluronidase, Proc. Soc. Exper. Biol. and Med. 64: 357 (Mar.) 1947.
- 445. Dorgeloh, J. R., and Tully, P. W.: Relationship of Boeck's sarcoid and tuberculosis; report of case in which tuberculosis of lymph nodes was associated with features highly suggestive of sarcoid, Arch. Path. 40: 309 (Nov.-Dec.) 1945.
- Dorinson, S. M., and Wagner, M. L.: An exact technic for clinically measuring and recording joint motion, Arch. Phys. Med. 29: 468 (Aug.) 1948.
- Dostrovsky, A.: Progressive scleroderma of the skin with cystic sclerodermal changes of the lungs, Arch. Dermat. and Syph. 55: 1 (Jan.) 1947.
- Dostrovsky, A., and Sagher, F.: Dermatomyositis and malignant tumour, Brit. J. Dermat. 58: 52 (Mar.-Apr.) 1946.
- 449. Douthwaite, A. H.: Problem of rheumatism, Practitioner 161: 153 (Sept.) 1948.
- Dowd, G. C.: Alpha tocopherol in the management of Sydenham's chorea, Ann. New York Acad. Sc. 52: 419 (Oct.) 1949.
- 451. Dowling, P. G.: Epidemic polyarthritis, M. I. Australia 1: 245 (Feb.) 1946.
- 452. Downing, J. G.: Yaws in Massachusetts, New England J. Med. 239: 17 (July) 1948.
- 453. Doyle, J. B.: Radicular pain in the upper extremity, California Med. 68: 255 (Apr.) 1948.
- Doyle, L. P., Andrews, F. N., and Hutchings, L. M.: The use of cortisone and ACTH in rheumatoid disease in swine, Proc. Soc. Exper. Biol. and Med. 74: 373 (June) 1950.
- 455. Draznin, S. Z., and Singer, K.: Legg-Perthes' disease (syndrome of many etiologies) with clinical and roentgenographic findings in a case of Gaucher's disease, Am. J. Roentgenol. 60: 490 (Oct.) 1948.
- Dresner, E., Pugh, L. G. C., and Wild, J. B.: ACTH in rheumatoid arthritis compared with intramuscular adrenaline and with deoxycortone and ascorbic acid, Lancet 1: 1149 (June) 1950.
- Druss, J. G.: Effusion in the temporomandibular joint complicated by otitis media, J. Mt. Sinai Hosp. 14: 931 (Jan.-Feb.) 1948.
- Dry, T. J., Butt, H. R., and Scheifley, C. H.: Effect of oral administration of paraaminobenzoic acid on concentration of salicylates in blood; preliminary report, Proc. Staff Meet., Mayo Clin. 21: 497 (Dec.) 1946; correction 22: 55 (Feb.) 1947.
- Dubow, E., and Solomon, N. H.: Salicylate tolerance and toxicity in children, Pediatrics 1: 495 (Apr.) 1948.
- Dudgeon, H. R., Jr.: Rupture of popliteal fascia, J. Bone and Joint Surg. 29: 522 (Apr.) 1947.
- Duemling, W. W.: Progressive disseminated coccidioidomycosis, Arch. Dermat. and Syph. 60: 781 (Nov.) (pt. 1) 1949.
- Duemling, W. W., and Horton, S. H., Jr.: Determination and treatment of penicillinresistant gonorrheal urethritis; report of 24 cases, U. S. Nav. M. Bull. 47: 605 (July-Aug.) 1947.
- Duff, G. L.: The diffuse collagen diseases; a morphologic correlation, Canad. M. A. J. 58: 317 (Apr.) 1948.

- Duncan, G. A.: Traumatic loose bodies from the patella, Virginia M. Monthly 73: 210 (May) 1946.
- Dunham, J., Rock, J., and Belt, E.: Isolation of filterable agent pathogenic for mice from case of Reiter's disease, J. Urol. 58: 212 (Sept.) 1947.
- Dunning, H. S.: Prognosis in so-called sciatic neuritis, Arch. Neurol. and Psychiat.
 55: 573 (June) 1946.
- Durbin, F. C.: Conservative treatment of sciatic pain by immobilization in plaster jacket, J. Bone and Joint Surg. 30B: 487 (Aug.) 1948.
- Duthie, J. J. R., and Swanson, J. N.: Clinical trial of para-amino-salicylic acid in the treatment of rheumatoid arthritis, Ann. Rheumat. Dis. 9: 132 (June) 1950.
- Dwindelle, J. H., Rein, C. R., Sternberg, T. H., and Sheldon, A. J.: Preliminary report on the evaluation of penicillin in the treatment of yaws, Am. J. Trop. Med. 26: 311 (May) 1946.
- Dworetzky, M., Code, C. F., and Higgins, G. M.: The effect of cortisone and ACTH on eosinophils and anaphylactic shock in guinea pigs, Proc. Soc. Exper. Biol. and Med. 75: 201 (Oct.) 1950.
- 471. East, T., and Oram, S.: The heart in scleroderma, Brit. Heart J. 9: 167 (July) 1947.
- 472. Eastwood, C. G.: Some aspects of chronic rheumatism, Gen. Practitioner 17: 105 (July)
- 473. Echols, D. H., and Rehfeldt, F. C.: Failure to disclose ruptured intervertebral disks in 32 operations for sciatica, J. Neurosurg. 6: 376 (Sept.) 1949.
- Echtman, J.: Painless treatment of ankylosed joints; report of 19 years' study, M. Rec. 159: 477 (Aug.) 1946.
- Eckert, C., and Decker, A.: Pathological studies of intervertebral discs, J. Bone and Joint Surg. 29: 447, 1947.
- 476. Edlund, T.: Absorption of protein and bacteria from normal and infected joints, Nature, London 161: 102 (Jan.) 1948.
- Edlund, T.: Studies on absorption of colloids and fluid from rabbit knee joints, Acta physiol. Scandinav. (supp. 62) 18: 1, 1949.
- Edlund, T., and Linderholm, H.: The effect of salyrgan (Mersalyl) on the resistance to movement of fluid through synovial membranes—an increased permeability of this connective tissue. Acta physiol. Scandinav. 21: 250, 1950.
- Edmonds, E. P.: Psychosomatic non-articular rheumatism, Ann. Rheumat. Dis. 6: 36 (Mar.) 1947.
- Edström, G.: Kinesotherapy and extension treatment in rheumatoid arthritis, Brit. J. Phys. Med. 10: 4 (Jan.-Feb.) 1947.
- Edström, G.: Rheumatoid arthritis in children; clinical study, Acta pædiat. 34: 339, 1947.
- Edström, G.: The effects of 2,3-dimercaptopropanol (BAL) on gold reactions, Ann. Rheumat. Dis. 9: 109 (June) 1950.
- 483. Edström, G., Lundin, G., and Wramner, T.: Investigations into the effect of hot, dry microclimate on peripheral circulation, etc., in arthritic patients, Ann. Rheumat. Dis. 7: 76 (June) 1948.
- 484. Edward, D. G. F., Crowley, N., Topley, E., and Moore, B.: An inquiry into the incidence of cross-infections, complications and return cases in scarlet fever, J. Hyg. 45: 251 (Aug.) 1947.
- 485. Edwards, C. M.: Polyarthritis in lambs following serum inoculation, Vet. Rec. 61: 95 (Feb.) 1949.
- 486. Edwards, E. G.: DeQuervain's stenosing tendo-vaginitis at the radial styloid process, South. Surgeon 16: 1081 (Nov.) 1950.
- Edwards, P. R., Bruner, D. W., and Moran, A. B.: Further studies on the occurrence and distribution of Salmonella types in the United States, J. Infect. Dis. 83: 220 (Nov.-Dec.) 1948.

Egelius, N., Havermark, N. G., and Jonsson, E.: Early symptoms of rheumatoid arthritis, Ann. Rheumat. Dis. 8: 217 (Sept.) 1949.

 Einbinder, J., and Schubert, M.: Separation of chondroitin sulfate from cartilage, J. Biol. Chem. 185: 725 (Aug.) 1950.

 Eisaman, J. L.: Anemia and cardiac cirrhosis from rheumatic heart disease, J. Indiana M. A. 40: 835 (Sept.) 1947.

 Eisele, C. W.: Some problems in the diagnosis of chronic brucellosis, M. Clin. North America 31: 182 (Jan.) 1947.

Eisele, C. W.: Current problems in the diagnosis and treatment of brucellosis, Wisconsin M. J. 49: 201 (Mar.) 1950.

 Eisenberg, H.: Alkaptonuria, ochronosis, arthritis and ruptured intervertebral disk; complicated by homologous serum reaction, Arch. Int. Med. 86: 79 (July) 1950.

494. Eisenberg, R. B., and Horn, R. C., Jr.: Synovial sarcoma of the chest wall; report of a case, Ann. Surg. 131: 281 (Feb.) 1950.

 Elftman, H., Elftman, A. G., and Zwemer, R. L.: Histochemical distribution of gold after administration of gold chloride, Anat. Rec. 96: 341 (Dec.) 1946.

 Elghammer, H. W.: Symposium on pediatrics; rheumatic fever, diagnostic criteria, and rheumatic heart disease, M. Clin. North America 30: 25 (Jan.) 1946.

497. Elkinton, J. R., Hunt, A. D., Godfrey, L., McCrory, W. W., Rogerson, A. G., and Stokes, J., Jr.: Effects of pituitary adrenocorticotropic hormone (ACTH) therapy, J. A. M. A. 141: 1273 (Dec.) 1949.

Ellman, P.: Morquio-Brailsford's disease simulating the arthritic manifestation of rheumatoid disease, Ann. Rheumat. Dis. 8: 267 (Dec.) 1949.

 Ellman, P., and Ball, R. E.: "Rheumatoid disease" with joint and pulmonary manifestations, Brit. M. J. 2: 816, 1948.

 Ellman, P., and Shaw, D.: The "chronic rheumatic" and his pains, Ann. Rheumat. Dis. 9: 341 (Dec.) 1950.

Elster, S. K.: Effect of ascorbic acid deficiency in collagen content of guinea pig tissues,
 J. Biol. Chem. 186: 105, 1950.

502. Elster, S. K., Freeman, M. E., and Anderson, P. R.: Effect of hyaluronidase on hematocrit and plasma proteins of albino rat, J. Lab. and Clin. Med. 34: 834 (June) 1949.

 Elwyn, D., and Sprinson, D. B.: Role of serine and acetate in uric acid formation, J. Biol. Chem. 184: 465 (June) 1950.

504. Empire Rheumatism Council, report by Scientific Advisory Committee: Controlled investigation into actiology and clinical features of rheumatoid arthritis, Brit. M. J. 1: 799 (Apr.) 1950.

505. Engel, D.: Trigger finger produced by excessive heat, Surgery 26: 659 (Oct.) 1949.

 Engel, M. B., Richmond, J. B., and Brodie, A. G.: Mandibular growth disturbance in rheumatoid arthritis of childhood, Am. J. Dis. Child. 78: 728 (Nov.) 1949.

507. Engle, J. P., Wakin, K. G., Erickson, D. J., and Krusen, F. H.: The effect of contrast baths on the peripheral circulation in patients with rheumatoid arthritis, Arch. Phys. Med. 31: 135 (Mar.) 1950.

Engleman, E.: Differential diagnosis of adult rheumatic fever and rheumatoid arthritis, California Med. 66: 227 (Apr.) 1947.

 Ensign, D. C., and Sigler, J. W.: The hands in arthritis, J. Michigan M. Soc. 49: 1078 (Sept.) 1950.

 Epstein, E.: Reiter's disease; comparison with keratosis blennorrhagica and with psoriasis arthropathica, Arch. Dermat. and Syph. 56: 191 (Aug.) 1947.

 Epstein, N., and Gardam, J. D.: A study of the Q-Tc interval in the electrocardiogram in rheumatic fever, J. Pediat. 36: 583 (May) 1950.

512. Epstein, N., Lubschez, R. L., deGara, P. F., and Wilson, M. G.: Immunologic and biochemical studies in infants and children with special reference to rheumatic fever; inhibition of hyaluronidase by sera, Pediatrics 4: 569 (Nov.) 1949.

- 513. Erdei, A.: Epidemic of acute lumbar pain, Canad. M. A. J. 59: 159 (Aug.) 1948.
- 514. Ergenbright, W. V., and Lowry, F. C.: Procaine injection for relief of pain in the hip, J. Bone and Joint Surg. 31A: 820 (Oct.) 1949.
- Erickson, D. J.: Physical medicine for the home-bound arthritic, Brit. J. Phys. Med. 13: 193 (Sept.) 1950.
- 516. Ettles, D. C. McC., Ellis, J. S., Young, R., Symonds, C., Roberts, I., and Williams, W. D.: Backache and sciatica in the army. Report of a discussion held at Cambridge Military Hospital, Aldershot, J. Roy. Army M. Corps 91: 137 (Oct.) 1948.
- 517. Evans, A. C.: Brucellosis in the United States, Am. J. Pub. Health 37: 139 (Feb.) 1947.
- Evans, J. A.: Reflex sympathetic dystrophy, Surg., Gynec. and Obst. 82: 36 (Jan.) 1946.
- Evans, J. A.: Sympathectomy for reflex sympathetic dystrophy; report of 29 cases, J. A. M. A. 132: 620 (Nov.) 1946.
- 520. Evans, J. A. P.: Discussion on the management of rheumatic fever and its early complications; oral penicillin in the prophylaxis of streptococcal infection and rheumatic relapse, Proc. Roy. Soc. Med. 43: 206 (Mar.) 1950.
- Evans, S. M.: Role of hypersensitivity in pathogenesis of rheumatic fever, Wisconsin M. J. 46: 783 (Aug.) 1947.
- Faber, V., and Schmith, K.: Determination of hyaluronidase inhibitor in serum, Scandinav. J. Clin. and Lab. Invest. 2: 298, 1950.
- Faber, V., and Schmith, K.: Variation in serum hyaluronidase inhibitor under administration of adrenocorticotropic hormone (ACTH), Scandinav. J. Clin. and Lab. Invest. 2: 303, 1950.
- 524. Fahey, J. J.: Progress in orthopedic surgery for 1946; a review prepared by an editorial board of the American Academy of Orthopedic Surgeons. Conditions involving the hip joint, Arch. Surg. 58: 89 (Jan.) 1949.
- 525. Falconer, M. A., McGeorge, M., and Begg, A. C.: Observations on the cause and mechanism of symptom-production in sciatica and low-back pain, J. Neurol., Neurosurg. and Psychiat. 11: 13 (Feb.) 1948.
- 526. Farber, H. R., Yiengst, M. J., and Shock, N. W.: The effect of therapeutic doses of aspirin on the acid-base balance of the blood in normal adults, Am. J. M. Sc. 217: 256 (Mar.) 1949.
- 527. Farley, R. T., and Spierling, H. F.: Arthritis therapy research; a 10 year report on use of natural food diet with vitamin "D," M. Times, New York 76: 435 (Oct.)
- Fawcitt, J.: Bone and joint changes associated with psoriasis, Brit. J. Radiol. 23: 440 (July) 1950.
- Fay, F. R.: Concerning calcinosis circumscripta with report of a case, M. J. Australia 2: 330 (Aug.) 1950.
- 530. Feffer, H., and Hirsh, H. L.: Pneumococcic arthritis; report of a case treated with penicillin, Ann. Int. Med. 25: 845 (Nov.) 1946.
- Felder, S. L., and Felder, L.: Unusual reaction to penicillin, J. A. M. A. 143: 361 (May) 1950.
- Ferguson, C., and Buchholtz, M.: Hyperpyrexia as an adjunct to chemotherapy, Mil. Surgeon 101: 20 (July) 1947.
- Ferguson, T.: Some industrial aspects of rheumatism, Practitioner 161: 170 (Sept.) 1948.
- Ferriman, D. G., and Wilsdon, R. B. N.: Adrenocorticotropic hormone in acute disseminated lupus erythematosus, Brit. M. J. 1: 884 (Apr.) 1950.
- 535. Fershtand, J. B., and Holsapple, C. K.: Rheumatoid arthritis with neutropenia, throm-bocytopenia, and splenomegaly (Felty's syndrome) with improvement after splenectomy, Texas J. Med. 46: 842 (Nov.) 1950.
- 536. Ficarra, B. J.: Traumatic etiology of Baker's cyst, Compens. Med. 2: 33 (Nov.) 1949.

537. Fields, A.: Cervical disk syndrome, Am. Pract. 2: 724 (July) 1948.

 Fields, A., and Hoesley, J.: Neck and shoulder pain, California Med. 70: 478 (June) 1949.

 Fincher, E. F.: Neurosurgical experiences in lumbago-sciatic syndrome, South. M. J. 39: 527 (July) 1946.

 Findlay, G. M.: Pleuropneumonia-like organisms and arthritis, Ann. Rheumat. Dis. 5: 153 (Sept.) 1946.

 Findlay, G. M., and Howard, E. M.: Coxsackie viruses and Bornholm disease, Brit. M. J. 1: 1233 (May) 1950.

 Finn, J. J., Jr.: Pleurodynia; preliminary note on epidemic in Boston, New England J. Med. 237: 621 (Oct.) 1947.

543. Finn, J. J., Jr., Weller, T. H., and Morgan, H. R.: Epidemic pleurodynia: clinical and etiologic studies based on 114 cases, Arch. Int. Med. 83: 305 (Mar.) 1949.

544. Finney, J. O., Boland, E. W., and Hench, P. S.: Precipitating and predisposing factors in rheumatoid arthritis [Proc. of Reunion Meeting, Amer. Rheumatism Assoc.], Ann. Rheumat. Dis. 6: 91 (June) 1947.

 Firtel, S. L.: Atypical and extensive myositis ossificans (case report), Bull. Hosp. Joint Dis. 8: 72 (Apr.) 1947.

 Fischel, E. E.: The role of allergy in the pathogenesis of rheumatic fever, Am. J. Med. 7: 772 (Dec.) 1949.

 Fischel, E. E.: Relationship of adrenal cortical activity to immune responses, Bull. New York Acad. Med. 26: 255 (Apr.) 1950.

548. Fischel, E. E., LeMay, M., and Kabat, E. A.: The effect of adrenocorticotrophic hormone and x-ray on the amount of circulating antibody, J. Immunol. 61: 89 (Jan.) 1949.

549. Fischel, E. E., and Pauli, R. H.: Serological studies; "phase" reaction and detection of autoantibodies in rheumatic state, J. Exper. Med. 89: 669 (June) 1949.

Fischel, E. E., Pauli, R. H., and Lesh, J.: Serologic studies in rheumatic fever. II.
 Serum complement in the rheumatic state, J. Clin. Investigation 28: 1172 (Sept.) 1049.

 Fischer, K. A., and Leatherman, K. D.: The nature of and treatment of tendinitis of the musculotendinous cuff of the shoulder and subacromial bursitis, South. Surgeon 16: 132 (Feb.) 1950.

552. Fischl, J. R.: Severe hypertrophic pulmonary osteo-arthropathy; report of a case due to carcinoma of the lung with operation and recovery, Am. J. Roentgenol. 64: 42 (July) 1950.

 Fischmann, E. J., and Gwynne, F. J.: The heart in rheumatoid arthritis, Brit. Heart J. 10: 125 (Apr.) 1948.

554. Fisher, A. M.: Some clinical features and pathological features observed in sarcoidosis, Tr. Am. Clin. and Climatol. A. (1947) 59: 58, 1948.

555. Fisher, G. S., and Moyer, J. B.: Hematologic phenomena as a test for acute disseminated lupus erythematosus, Grace Hosp. Bull. 28: 3 (Jan.) 1950.

 Fisk, G. H., Howard, R. P., and Fay, K.: Clinical effects of testosterone and pregnenolone therapy, Canad. M. A. J. 63: 342 (Oct.) 1950.

 FitzPatrick, W. J., and Schwartz, S. O.: Aplastic anemia secondary to gold therapy; case report, Blood 3: 192 (Feb.) 1948.

 Flashman, F. L., and Ghormley, R. K.: Osteochondritis dissecans of the head of the femur, West. J. Surg. 57: 221 (June) 1949.

 Fletcher, E.: The diagnosis and modern treatment of early ankylosing spondylitis, M. Press 221: 451 (May) 1949.

 Fletcher, E.: Osteoarthritis and its treatment, Brit. J. Phys. Med. 11: 135 (Sept.-Oct.) 1948.

- Fletcher, E. T. D.: Symposium on rheumatic disorders; ankylosing spondylitis, Clin. J. 79: 90 (Apr.) 1950.
- 562. Fletcher, G. H.: Backward displacement of fifth lumbar vertebra in degenerative disc disease; significance of difference in anteroposterior diameters of fifth lumbar and first sacral vertebrae, J. Bone and Joint Surg. 29: 1019 (Oct.) 1947.
- Flood, J. M., and DeLaney, J. J.: Acute disseminated lupus erythematosus; a case report. Guthrie Clin. Bull. 20: 31 (July) 1950.
- 564. Flynn, J. E.: Acute suppurative tenosynovitis of the hand, New England J. Med. 242: 241 (Feb.) 1950.
- Flynn, J. E., and Irish, O. J.: Blood sugar level following intravenous glucose in rheumatoid arthritis. Science 104: 344 (Oct.) 1946.
- Foged, J.: Temporomandibular arthrosis (with eracking or snapping), Lancet 2: 1209 (Dec.) 1949.
- Foldes, J.: Acute systemic lupus erythematosus, Am. J. Clin. Path. 16: 160 (Mar.) 1946.
- 568. Follis, R. H., Jr.: Phosphatase activity of cartilage and periosteum with various substrates, Bull. Johns Hopkins Hosp. 87: 181 (Sept.) 1950.
- 569. Forbes, D.: Case of Reiter's disease, Brit. M. J. 2: 859 (Dec.) 1946.
- Forbus, W. D., and Bestebreurtje, A. M.: Coccidioidomycosis; a study of 95 cases of disseminated type with special reference to pathogenesis of the disease, Mil. Surgeon 99: 653 (Nov.) 1946.
- Ford, L. T., and Key, J. A.: An evaluation of myelography in the diagnosis of intervertebral-disc lesions in the low back, J. Bone and Joint Surg. 32A: 257 (Apr.) 1950.
- 572. Ford, W. J.: Neostigmine in arthritis; a case with toxic reaction, Quart. Bull., Northwestern Univ. M. School 22: 125, 1948.
- Forestier, J., Certonciny, A., and Jacqueline, F.: Therapeutic value of copper salts in rheumatoid arthritis, Stanford M. Bull. 8: 12 (Feb.) 1950.
- Forestier, J., and Rotes-Querol, J.: Senile ankylosing hyperostosis of the spine, Ann. Rheumat. Dis. 9: 321 (Dec.) 1950.
- Forman, B., and Lewey, F. H.: A mechanical joint mobilizer, Physiotherapy Rev. 27: 370 (Dec.) 1947.
- Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G.: Clinical studies with pituitary adrenocorticotropin, J. Clin. Endocrinol. 8: 15 (Jan.) 1948.
- 577. Forsham, P. H., Thorn, G. W., Bergner, G. E., and Emerson, K., Jr.: Metabolic changes induced by synthetic 11-dehydrocorticosterone acetate, including comparative studies with synthetic desoxycorticosterone acetate, natural 17-hydroxycorticosterone and lipo-adrenal cortex (preliminary report), Am. J. Med. 1: 105 (Aug.) 1946.
- Forsyth, H. F., Dillard, P. H., and Moore, R. A.: Causalgia; its etiology, diagnosis and treatment with tetra-ethyl-ammonium chloride (etamon chloride), North Carolina M. J. 8: 659 (Oct.) 1947.
- 579. Foster, D. B., and Bassett, R. C.: Neurogenic arthropathy (Charcot joint) associated with diabetic neuropathy; report of 2 cases; Arch. Neurol. and Psychiat. 57: 173 (Feb.) 1947.
- Foster, L. N.: Benign giant cell tumor of tendon sheaths; example of sclerosing hemangioma, Am. J. Path. 23: 567 (July) 1947.
- Fourman, P., Bartter, F. C., Fuller, A., Dempsey, E., Carroll, E., and Alexander, J.: Effects of 17-hydroxy-corticosterone ("compound F") in man, J. Clin. Investigation 29: 1462 (Nov.) 1950.
- 582. Fox, H.: Generalized, progressive scleroderma associated with changes in the lungs, the larynx, and the esophagus, Arch. Dermat. and Syph. 55: 269 (Feb.) 1947.
- 583. Francisco, R.: Rheumatic heart disease in the tropics with special reference to its incidence in Puerto Rico, Clinics 5: 971 (Dec.) 1946.

 Franks, A. G.: Successful combined treatment of penicillin-resistant gonorrhea, Am. J. M. Sc. 211: 553 (May) 1946.

 Fraser, T. N.: Ankylosing spondylitis in sisters, Ann. Rheumat. Dis. 9: 231 (Sept.) 1950.

Fraser, T. N.: Flocculation tests in rheumatoid arthritis, Ann. Rheumat. Dis. 7: 83
 (June) 1948.

 Freedberg, A. S., McManus, M. J., and Altschule, M. D.: Electrocardiogram in man during episode of chill and fever induced by intravenous typhoid vaccine, Am. Heart J. 34: 249 (Aug.) 1947.

588. Freeman, H., Pincus, G., Johnson, C. W., Bachrach, S., McCabe, G. E., and MacGilpin, H.: Therapeutic efficacy of Δ-5-pregnenolone in rheumatoid arthritis; preliminary observations, J. A. M. A. 142: 1124 (Apr.) 1950.

589. Freeman, J. T.: Ehlers-Danlos syndrome, Am. J. Dis. Child. 79: 1049 (June) 1950.

 Freeman, S., Rhoads, P. S., and Yeager, L. B.: Toxic manifestations associated with prolonged ertron ingestion, J. A. M. A. 130: 197 (Jan.) 1946.

 Freiman, D. G.: Medical progress; sarcoidosis, New England J. Med. 239: 664 (Oct.) 1948; 709 (Nov.) 1948; 743 (Nov.) 1948.

 Freireich, A. W., Schwartz, S., and Steinbrocker, O.: Penicillin in the treatment of keratosis blennorrhagica with polyarthritis, Arch. Int. Med. 79: 239 (Feb.) 1947.

593. Freud, P., Rook, G. D., and Brunhofer, A.: Reactivation of rheumatic fever by small-pox vaccination, J. Pediat. 36: 635 (May) 1950.

Freud, P., Weisz, A., and Brunhofer, A.: Miliary tuberculosis simulating acute rheumatic fever, Am. J. Dis. Child. 79: 676 (Apr.) 1950.

 Freund, H. A., Basinski, D. H., and Scott, R. B.: 17-keto-steroid excretion in rheumatoid arthritis, J. Michigan M. Soc. 49: 1076 (Sept.) 1950.

Freund, H. A., and Stulberg, C. S.: The hemagglutination test for rheumatoid arthritis,
 J. Michigan M. Soc. 49: 1084 (Sept.) 1950,

 Freyberg, R. H.: Effects of cortisone and ACTH in rheumatoid arthritis, Bull. New York Acad. Med. 26: 206 (Apr.) 1950.

 Freyberg, R. H.: Present status of gold therapy for rheumatoid arthritis, J. A. M. A. 143: 418 (June) 1950.

 Freyberg, R. H.: Roentgen therapy for rheumatic diseases, M. Clin. North America 30: 603 (May) 1946.

Freyberg, R. H.: "Focal infection" in relation to rheumatic diseases; critical appraisal,
 J. Am. Dent. A. 33: 1101 (Sept.) 1946.

 Freyberg, R. H.: Practical considerations in the management of arthritis, Pennsylvania M. J. 51: 729 (Apr.) 1948.

602. Freyberg, R. H.: The use of cortisone and ACTH in rheumatoid arthritis, Bull. Rheumat. Dis. 1: 1 (Sept.) 1950.

Freyberg, R. H., Traeger, C. T., Adams, C. H., Kuscu, T., Wainerdi, H., and Bonomo,
 I.: Effectiveness of cortisone administered orally, Science 112: 429 (Oct.) 1950.

604. Friedenberg, Z. B.: Osteitis pubis with involvement of the hip joint, J. Bone and Joint Surg. 32A: 924 (Oct.) 1950.

605. Friedman, H. H., and Steinbrocker, O.: Intensive chrysotherapy (with lauron) in rheumatoid arthritis, New England J. Med. 240: 362 (Mar.) 1949.

Friedman, M.: Effect of glycine on production and excretion of uric acid, J. Clin. Investigation 26: 815 (July) 1947.

607. Friedman, M., and Byers, S. O.: Effect of sodium salicylate on uric acid clearance of Dalmatian dog, Am. J. Physiol. 154: 167 (July) 1948.

608. Friedman, M., and Byers, S. O.: Observations concerning the causes of excess excretion of uric acid in the Dalmatian dog, J. Biol. Chem. 175: 727, 1948.

 Friedman, M. S.: Xanthoma of Achilles tendon, J. Bone and Joint Surg. 29: 760 (July) 1947.

- 610. Friedman, P. S.: Roentgen treatment and roentgen diagnosis of the painful shoulder, Am. Pract. and Digest Treat. 1: 1133 (Nov.) 1950.
- Friedman, S., and Harris, T. N.: Apical diastolic heart sounds in active rheumatic fever, Pediatrics 3: 603 (May) 1949.
- 612. Friedmann, I., and Por, F.: Acute interstitial polymyositis treated with penicillin, Brit. M. J. 2: 494 (Sept.) 1947.
- 613. Frost, J. W., Sunderman, F. W., and Leopold, I. S.: Prolonged hypercalcemia and metastatic calcification of the sclera following the use of vitamin D in the treatment of rheumatoid arthritis, Am. J. M. Sc. 214: 639 (Dec.) 1947.
- 614. Fulton, J. K., Marcus, S., and Robinson, W. D.: Hyaluronidase inhibitors in body fluids in normal and disease states, Proc. Soc. Exper. Biol. and Med. 69: 258 (Nov.) 1948.
- 615. Furcolow, M. L., Bunnell, I. L., and Tenenberg, D. J.: A complement fixation test for histoplasmosis; preliminary results with human sera, Pub. Health Rep. 63: 169 (Feb.) 1948.
- 616. Furlong, J. J.: The differential diagnosis of rheumatism; a clinical study of 500 cases, California Med. 70: 472 (June) 1949.
- Galluccio, A. C.: Spondylolisthesis; further remarks with emphasis on radiologic aspects, Radiology 46: 356 (Apr.) 1946.
- 618. Galpine, J. F.: A case of abortus infection treated with "aureomycin," Brit. M. J. 1: 1037 (June) 1949.
- 619. Gama, C.: Neuralgic pain wrongly ascribed to posterior hernia of intervertebral disks; 2 cases, J. Internat. Coll. Surgeons 13: 578 (May) 1950.
- Gardner, E.: Nerve supply of diarthrodial joints, Stanford M. Bull. 6: 367 (Aug.) 1948.
- 621. Gardner, E.: The innervation of the elbow joint, Anat. Rec. 102: 161 (Oct.) 1948.
- 622. Gardner, E.: Physiology of movable joints, Physiol. Rev. 30: 127 (Apr.) 1950.
- 623. Gardner, G. M., Fairley, De L. M., and Kuzell, W. C.: Effect of BAL on experimental polyarthritis of rats, Proc. Soc. Exper. Biol. and Med. 71: 130 (May) 1949.
- 624. Gauld, W. R.: Hypersplenism with arthritis; case, Lancet 2: 989 (Nov.) 1949.
- 625. Gelber, L. J.: X-ray therapy of arthritis and bursitis, M. Rec. 160: 344 (June) 1947. 626. Gelfand, M.: Tropical myositis and idiopathic thrombophlebitis (tropical primary phle-
- bitis), Tr. Roy. Soc. Trop. Med. and Hyg. 43: 439 (Jan.) 1950. 627. Gelfand, M.: Tropical phlebitis and its relation to myositis tropica, J. Trop. Med. 52:
- 248 (Dec.) 1949. 628. Gelfand, M. L.: Allergic reaction to penicillin, New York State J. Med. 47: 2707 (Dec.)
- 1947.
 629. Gelfand, M. L., and Aronoff, S.: Periarteritis nodosa—possible relation to the increased
- usage of sulfonamides, Ann. Int. Med. 30: 919 (May) 1949.
 630. Gellman, M.: Arthrodesis of the elbow; preliminary report of a new operation, J. Bone
- and Joint Surg. 29: 850 (Oct.) 1947.
 631. Geren, W., Bendich, A., Bodansky, O., and Brown, G. B.: Fate of uric acid in man, J.
- Biol. Chem. 183: 21 (Mar.) 1950.
 632. Gershman, M.: Tuberculosis of the short bones of the hand, Quart. Bull., Sea View Hosp. 10: 146 (Oct.) 1948.
- 633. Gervis, W. H.: Excision of trapezium for osteoarthritis of trapeziometacarpal joint, J. Bone and Joint Surg. 31B: 537 (Nov.) 1949.
- 634. Gezon, H. M.: Antibiotic studies on beta hemolytic streptococci; penicillin resistance acquired by group A organisms, Proc. Soc. Exper. Biol. and Med. 67: 208, 1948.
- 635. Ghormley, R. K.: Degenerative changes of the knee joint following internal derangement, J. Iowa M. Soc. 38: 88 (Mar.) 1948.
- 636. Ghormley, R. K.: Late joint changes as a result of internal derangements of the knee, Am. J. Surg. 76: 496 (Nov.) 1948.
- 637. Ghormley, R. K., and Clegg, R. S.: Bone and joint changes in hemophilia, with report

of cases of so-called hemophilic pseudotumor, J. Bone and Joint Surg. 30A: 589 (July) 1948.

- 638. Gibson, H. J.: Blood sedimentation rate in rheumatoid arthritis and allied conditions, Practitioner 157: 28 (July) 1946.
- 639. Gibson, H. J., and Shiers, D.: A controlled series of Cooke-Arneth polynuclear counts in rheumatoid arthritis, Ann. Rheumat. Dis. 7: 100 (June) 1948.
- Gibson, S.: Clinical manifestations of rheumatic fever; determination of rheumatic activity, J. Michigan M. Soc. 45: 193 (Feb.) 1948.
- 641. Gilbert, J. T., Jr., and Moore, F. H.: Gold therapy in rheumatoid arthritis, J. Kentucky M. A. 48: 308 (July) 1950.
- 642. Gilchrist, K. J.: Suppurative arthritis of the hip joint treated with penicillin; report of 4 cases, Brit. M. J. 2: 450 (Sept.) 1947.
- 643. Gillespie, H. W.: Further observations on radiological diagnosis of lumbar intervertebral disk lesions, Brit. J. Radiol. 20: 37 (Jan.) 1947; correction 20: 70 (Feb.) 1947.
- 644. Gillman, T., and Gillman, J.: Value of Speransky's method of spinal pumping in the treatment of rheumatic fever and rheumatoid arthritis, Am. J. M. Sc. 211: 448 (Apr.) 1946.
- 645. Ginsburg, M.: Palindromic rheumatism: effective treatment with gold, Ohio State M. J. 44: 707 (July) 1948.
- Glazebrook, A. J., and Wrigley, F.: Clinical trials of succinates and of heparin in rheumatic fever, Brit. M. J. 2: 789 (Oct.) 1949.
- 647. Glick, D., Bieter, R. N., and Wright, H. N.: Mucolytic enzyme systems; effect of certain quinolines on hyaluronidase and its serum inhibitor, Proc. Soc. Exper. Biol. and Med. 74: 778 (Aug.) 1950.
- 648. Glick, D., Good, R. A., Kelley, V., Winzler, C., and Mehl, J. W.: Lack of identity of hyaluronidase inhibitor and certain mucoproteins in blood serum, Proc. Soc. Exper. Biol. and Med. 71: 412 (July) 1949.
- 649. Glick, D., and Kaufmann, M.: Mucolytic enzyme systems. XIII. Effect of compounds on hyaluronidase and its inhibition by human serum, Proc. Soc. Exper. Biol. and Med. 74: 279 (June) 1950.
- Glick, D., and Moore, D. H.: Hyaluronidase inhibitor in electrophoretically separated fractions of human serum, Arch. Biochem. 19: 173, 1948.
- 651. Glick, H., Todd, R., Detwiler, R. H., McLendon, P. A., Copeland, E., and Walsh, B.: Rheumatoid arthritis with associated cardiac involvement; case, Clin. Proc. Child. Hosp. 3: 268 (Oct.) 1947.
- 652. Glover, J. A.: Acute rheumatism, Ann. Rheumat. Dis. 5: 126 (June) 1946.
- 653. Glover, J. A.: Decline of mortality from rheumatic fever, Month. Bull. Min. Health and Emerg. Pub. Health Lab. Serv. 5: 222 (Oct.) 1946.
- 654. Godfrey, M. F.: X-ray diagnosis and therapy in arthritis, California Med. 69: 16 (July) 1948.
- 655. Godfrey-Smith, R. A.: Reiter's syndrome, M. J. Australia 2: 574 (Nov.) 1947.
- 656. Godlowski, Z. Z.: Stimulation of the suprarenal glands in the treatment of rheumatoid arthritis; preliminary report, Ann. Rheumat. Dis. 8: 285 (Dec.) 1949.
- 657. Goerner, J. R., Massell, B. F., and Jones, T. D.: Use of penicillin in the treatment of carriers of beta-hemolytic streptococci among patients with rheumatic fever, New England J. Med. 237: 576 (Oct.) 1947.
- 658. Goldberg, H. C.: Differential diagnosis of sulfa drug reactions, J. M. Soc. New Jersey 43: 87 (Mar.) 1946.
- 659. Golden, A., Bondy, P. K., and Sheldon, W. H.: Pituitary basophile hyperplasia and Crooke's hyaline changes in man after ACTH therapy, Proc. Soc. Exper. Biol. and Med. 74: 455 (June) 1950.
- 660. Golden, P. B., Meyerding, H. W., and Dockerty, M. B.: Articular vascular leiomyoma; report of a case, Proc. Staff Meet., Mayo Clin. 24: 414 (Aug.) 1949.

662. Goldman, H.: Lymphogranuloma venereum, Bull. Hosp. Joint Dis. 9: 147 (Oct.) 1948.
663. Goldman, L.: Intensive panthenol therapy of lupus erythematosus, J. Invest. Dermat.

15: 291 (Oct.) 1950.

- 664. Goldman, R., Adams, W. S., Beck, W. S., Levin, M., Bassett, S. H., and White, A.: The effect of ACTH on one case of periarteritis nodosa, Proc. First Clinical ACTH Conference, 1950, Blakiston Co., Philadelphia, p. 437.
- 665. Goldstein, A. E., and Rubin, S. W.: Reiter's disease followed by true infective abacterial pyuria, Brit. J. Urol. 19: 32 (Mar.) 1947.
- 666. Goldstein, K.: Analysis of 200 cases of arthritis admitted to an army general hospital, New York State J. Med. 46: 727 (Apr.) 1946.
- 667. Gonyea, L. M., Kallsen, R. A., and Marlow, A. A.: The occurrence of "L. E." cell in clotted blood, J. Invest. Dermat. 15: 11 (July) 1950.
- 668. Good, M. G.: Acroparaesthesia—an idiopathic myalgia of elbow, Edinburgh M. J. 56: 366 (Aug.) 1949.
- 669. Good, R. A., and Campbell, B.: Relationship of bone marrow plasmacytosis to the changes in serum gamma globulin in rheumatic fever, Am. J. Med. 9: 330 (Sept.) 1950.
- 670. Good, R. A., and Glick, D.: Mucolytic enzyme systems. IX. Nonspecific hyaluronidase inhibitor in rheumatic fever, J. Infect. Dis. 86: 38 (Jan.-Feb.) 1950.
- 671. Good, R. A., Good, T. A., Kelley, V. C., and Glick, D.: Response of the serum level of hyaluronidase inhibitor and mucoprotein to stress, Federation Proc. 9: 178, 1950.
- 672. Goodman, M. J.: Periarteritis nodosa with recovery; report of an unusual case apparently due to sensitivity to sulfadiazine, Ann. Int. Med. 28: 181 (Jan.) 1948.
- 673. Goodman, R. D.: Multiple Charcot joints, Am. J. Roentgenol. 62: 531 (Oct.) 1949.
- 674. Goodwin, J. F.: Tuberculous arthralgia, Post-Grad. M. J. 22: 200 (July) 1946.
- 675. Gordon, E. J., and Shechter, N.: Salmonella suipestifer pyarthrosis of knee, J. Bone and Joint Surg. 30A: 220 (Jan.) 1948.
- Gordon, G. L.: Development of refractory state to adrenocorticotropic hormone, Endocrinology 45: 571 (Dec.) 1949.
- 677. Gordon, G. L.: Osseous Gaucher's disease; report of 2 cases in siblings, Am. J. Med. 8: 332 (Mar.) 1950.
- 678. Gordon, H. S., Hoffman, S. J., Schultz, A., and Lomberg, F.: Serous arthritis of the knee joint; report of a case caused by Salmonella typhosa and Salmonella montevideo in a child, J. A. M. A. 141: 469 (Oct.) 1949.
- 679. Gordon, M.: Is rheumatism a virus disease? Lancet 1: 697 (May) 1948.
- 680. Gore, I., and Isaacson, N. H.: The pathology of hyperpyrexia; observations at autopsy in 17 cases of fever therapy, Am. J. Path. 25: 1029 (Sept.) 1949.
- Goren, M. L.: Localized coccidioidomycosis of bone; report of case, J. Bone and Joint Surg. 28: 157 (Jan.) 1946.
- 682. Gorrell, R. L.: Musculofascial pain; treatment by local injection of analgesic drugs, J. A. M. A. 142: 557 (Feb.) 1950.
- 683. Goslings, J., Hijmans, W. H., van Limpt, P. M., and van Gilse, H. A.: Prolonged treatment of rheumatoid arthritis with ACTH alone and with gold, Brit. M. J. 2: 1019 (Nov.) 1950.
- 684. Goswell, G.: Further report of epidemic of acute polyarthritis, M. J. Australia 2: 861 (Dec.) 1946.
- 685. Gottlieb, C., Sharlin, H. S., and Feld, H.: Hypertrophic pulmonary osteoarthropathy, J. Pediat. 30: 462 (Apr.) 1947.
- Gottschalk, L. A., Serota, H. M., and Roman, K. G.: Handwriting in rheumatoid arthritics, Psychosom. Med. 11: 354 (Nov.-Dec.) 1949.
- 687. Gottschalk, L. A., Serota, H. M., and Shapiro, L. B.: Psychological conflict and neuro-muscular tension; preliminary report and method, as applied to rheumatoid arthritis.

A. Research Nerv. and Ment. Dis. Proc. (1949) 29: 735, 1950; Psychosom. Med. 12: 315 (Sept.-Oct.) 1950.

- 688. Grace, A. W., and Combes, F. C.: Remission of disseminated lupus erythematosus induced by adrenocorticotropin, Proc. Soc. Exper. Biol. and Med. 72: 563 (Dec.) 1949.
- 689. Graef, I., Hickey, D. V., and Altmann, V.: Cardiac lesions in rheumatoid arthritis. Am. Heart J. 37: 635, 1949.
- 690. Graffin, J. W., Taylor, C. B., and Hass, G. M.: A clinical and pathologic study of disseminated lupus erythematosus, M. Clin. North America 33: 79 (Jan.) 1949.
- Graham, D. C.: Rehabilitation of arthritic, Treat. Serv. Bull. 5: 488 (Nov.) 1950.
 Graham, G. S., Jr.: Still-Chauffard syndrome; rheumatoid arthritis with systemic manifestations, J. M. A. Alabama 15: 323 (May) 1946.
- Graham, J. D. P., and Parker, W. A.: The toxic manifestations of sodium salicylate therapy, Quart. J. Med. 17: 153 (Apr.) 1948.
- 694. Graham, W., Hunt, T. E., and Mowat, D.: Rheumatoid arthritis; result of treatment with desoxycorticosterone acetate and ascorbic acid (arthrodox), Canad. M. A. J. 63: 121 (Aug.) 1950.
- 695. Graham, W., and Ogryzlo, M. A.: Ankylosing (Marie-Strümpell) spondylitis (analysis of 100 cases), Canad. M. A. J. 57: 16 (July) 1947.
- 696. Grais, M. L., and Glick, D.: Mucolytic enzyme systems; inhibition of hyaluronidase by serum in infectious diseases, J. Infect. Dis. 85: 101 (July-Aug.) 1949.
- 697. Granirer, L. W.: The effect of antireticular cytotoxic serum on patients with osteoarthritis, New York State J. Med. 49: 1067 (May) 1949.
- 698. Granirer, L. W.: A study of the lipids in postpartum plasma: its use in rheumatoid arthritis, Surg., Gynec. and Obst. 91: 591 (Nov.) 1950.
- 699. Granirer, L. W.: Pericardial effusion in rheumatoid arthritis, M. Clin. North America 30: 562 (May) 1946.
- Granirer, L. W.: Cholesterol content of urine in arthritis, M. Clin. North America 30: 645 (May) 1946.
- Granirer, L. W., and Victor, A. W.: The beneficial effect of postpartum plasma in a case of psoriatic arthritis; preliminary report, M. Clin. North America 33: 907 (May) 1949.
- 702. Grant, F. C., Austin, G., Friedenberg, Z., and Hansen, A.: A correlation of neurologic, orthopedic, and roentgenographic findings in displaced intervertebral discs, Surg., Gynec, and Obst. 87: 561 (Nov.) 1948.
- Graubard, D. J., Kovacs, J., and Ritter, H. H.: Management of destructive arthritis of hip by means of intravenous procaine, Ann. Int. Med. 28: 1106 (June) 1948.
- 704. Graubard, D. J., and Peterson, M. C.: Intravenous use of procaine in the management of arthritis, J. A. M. A. 141: 756 (Nov.) 1949.
- 705. Gray, C.: Chondromalacia, Brit. M. J. 1: 427 (Mar.) 1948.
- Gray, F. G.: Spontaneous cardiac lesions in mice; their bearing on attempts to produce experimental carditis, Am. J. Path. 25: 1215 (Nov.) 1949.
- Green, J. R., Doerner, A. A., and Gordon, E. M.: The use of intravenous procaine in the treatment of arthritis, New Orleans M. and S. J. 102: 525 (May) 1950.
- Greenebaum, J. V., Freiberg, J. A., and Saenger, E. L.: Pyarthrosis in infancy; report of a case with the review of the literature, Ohio M. J. 45: 453 (May) 1949.
- Greenblatt, R. B.: Socioeconomic aspects of granuloma inguinale, J. Ven. Dis. Inform. 28: 181 (Sept.) 1947.
- Greenblatt, R. B., and Kupperman, H. S.: Menopausal arthritis, M. Clin. North America 30: 576 (May) 1946.
- Greenfield, M. M., and Wallace, K. M.: Pigmented villonodular synovitis, Radiology 54: 350 (Mar.) 1950.
- 712. Greenough, E. E.: Chloromycetin in the treatment of rheumatoid arthritis; a preliminary report, South Dakota J. Med. and Pharm. 3: 139 (May) 1950.

- 713. Greer, C., and Withers, B. T.: Review of Costen's temporomandibular joint syndrome; report of a typical case, Texas Rep. Biol. and Med. 6: 23, 1948.
- 714. Gregory, J. E.: The experimental production of periarteritis nodosa, rheumatic carditis and rheumatic pneumonitis, Pediatrics 2: 703 (Dec.) 1948.
- Griffith, G. C.: Rheumatic fever; its recognition and treatment, J. A. M. A. 133: 974 (Apr.) 1947.
- Griffith, G. C.: A community program for the control of rheumatic fever, California Health 6: 65 (Oct.) 1948.
- 717. Griffith, G. C.: The epidemiology of rheumatic fever; public health aspects, Am. J. Pub. Health 38: 682 (May) (pt. 1) 1948.
- Griffith, G. C., and Campbell, A. D.: Skin manifestations of rheumatic fever, Am. Pract. 2: 622 (May) 1948.
- Griffith, G. C., and Halley, E. P.: Treatment of rheumatic fever by roentgen-ray irradiation, Ann. Int. Med. 24: 1039 (June) 1946.
- Griffith, G. C., and Huntington, R. W., Jr.: Sudden death in rheumatic fever, Ann. Int. Med. 25: 283 (Aug.) 1946.
- Griffith, G. C., Moore, F. J., McGinn, S., and Cosby, R. S.: The familial incidence of rheumatic fever; a statistical study of the familial and personal history of rheumatic fever, Am. Heart J. 35: 444 (Mar.) 1948.
- Griggs, J. F., and Case, L. W.: Variations in brucella agglutination reactions in different laboratories, Am. J. Clin. Path. 18: 506 (June) 1948.
- 723. Groen, J., and Garrer, A. H.: Adult Gaucher's disease with special reference to the variations in its clinical course and the value of sternal puncture as an aid to its diagnosis, Blood 3: 1221, 1948.
- Gross, J.: A study of certain connective tissue constituents with the electron microscope, Ann. New York Acad. Sc. 52: 964 (May) 1950.
- Gross, J., and Schmitt, F. O.: The structure of human skin collagen as studied with the electron microscope, J. Exper. Med. 88: 555 (Nov.) 1948.
- Grossman, M.: Coordinating occupational therapy and physical medicine in Veterans Administration hospitals, Occup. Therapy 25: 118 (Aug.) 1946.
- Grott, J. W.: Musculo-articular pains in light of figures pertaining to oxalic and uric acid in blood, Acta med. Scandinav. 125: 576, 1946.
- Gruca, A.: Treatment of quiescent tuberculosis by excision and "dynamic" osteotomy.
 J. Bone and Joint Surg. 32B: 174 (May) 1950.
- 729. Gruenwald, P.: Visceral lesions in a case of rheumatoid arthritis, Arch. Path. 46: 59
 (July) 1948.
- Gryboski, J. S.: Palindromic rheumatism, Bull. U. S. Army M. Dept. 8: 550 (July) 1948.
- Gueft, B.: Depolymerization of nucleic acid in acute disseminated lupus erythematosus, Arch. Dermat. and Syph. 61: 892 (June) 1950.
- 732. Guerra, F.: The action of sodium salicylate and sulfadiazine on hyaluronidase, J. Pharmacol. and Exper. Therap. 87: 193, 1946.
- Guerra, F.: Hyaluronidase inhibition by sodium salicylate in rheumatic fever, Science 103: 686 (June) 1946.
- 734. Guest, C. M., Kammerer, W. H., Cecil, R. L., and Berson, S. A.: Epinephrine, pregnenolone and testosterone in the treatment of rheumatoid arthritis and gout, J. A. M. A. 143: 338 (May) 1950.
- Gunter, G. S.: The determination of "Spinnbarkeit" of synovial fluid and its destruction by enzymic action, Australian J. Exper. Biol. and M. Sc. 27: 265, 1949.
- 736. Gurdjian, E. S., and Webster, J. E.: Lumbar herniations of the nucleus pulposus; an analysis of 196 operated cases, Am. J. Surg. 76: 235 (Sept.) 1948.
- 737. Guri, J. P.: Pyogenic osteomyelitis of the spine; differential diagnosis through clinical and roentgenographic observations, J. Bone and Joint Surg. 28: 29 (Jan.) 1946.

 Guri, J. P.: Formation and significance of vertebral ankylosis in tuberculous spines, J. Bone and Joint Surg. 29: 136 (Jan.) 1947.

 Guss, J. H.: Scleroderma with unusual central nervous system manifestations, Virginia M. Monthly 74: 454 (Oct.) 1947.

 Gutman, A. B., and Yu, T. F.: Effects of adrenocorticotropic hormone (ACTH) in gout, Am. J. Med. 9: 24 (July) 1950.

741. Guy, P. F.: Diagnosis of rheumatic fever, Northwest Med. 46: 38 (Jan.) 1947.

742. Habif, D. V., Hare, C. C., and Glaser, G. H.: Perforated duodenal ulcer associated with pituitary adrenocorticotropic hormone (ACTH) therapy, J. A. M. A. 144: 996 (Nov.) 1950.

 Hackett, C. J.: Review of references to the bone lesions of yaws, Trop. Dis. Bull. 43: 1091 (Dec.) 1946.

744. Hadidian, Z., and Pirie, N. W.: The preparation and some properties of hyaluronic acid from human umbilical cord, Biochem. J. 42: 260, 1948.

 Hadley, L. A.: Accessory sacroiliac articulations with arthritic changes, Radiology 55: 403 (Sept.) 1950.

 Hagemann, P. O.: Gout; review of diagnosis and management, J. Missouri M. A. 45: 192 (Mar.) 1948.

Haggart, G. E.: Surgical treatment of degenerative arthritis of knee joint, New England J. Med. 236: 971 (June) 1947.

 Haggart, G. E.: Value of conservative management in cervicobrachial pain, J. A. M. A. 137: 508 (June) 1948.

 Haggart, G. E., and Winter, E. F.: de Quervain's disease: stenosing tendovaginitis over the radial styloid, S. Clin. North America 28: 817 (June) 1948.

 Hakanson, E. Y., and Glick, D.: Mucolytic enzyme systems; inhibition of hyaluronidase by human blood serum during normal menstrual cycle and pregnancy, J. Clin. Investigation 28: 713 (July) 1949.

 Haldeman, K. O., and Soto-Hall, R.: The response of articular cartilage to trauma; with special reference to the knee joint, California Med. 69: 179 (Sept.) 1948.

Haley, J. C., and Perry, J. H.: Protrusions of intervertebral discs; study of their distribution, characteristics, and effects on the nervous system, Am. J. Surg. 80: 394 (Oct.) 1950.

753. Hall, I. M.: Sarcoidosis, Post-Grad. M. J. 23: 233 (May) 1947.

754. Hall, W. H.: Brucellosis-clinical aspects, Minnesota Med. 29: 679 (July) 1946.

 Hall, W. K., Hawkins, K. R., and Child, G. P.: The inheritance of alkaptonuria in a large American family, J. Hered. 41: 23 (Jan.) 1950.

 Hallberg, L.: Effects of deoxycortone and methylene-blue in rheumatoid arthritis; an attempt to explain the action of ascorbic acid on deoxycortone, Lancet 1: 351 (Feb.) 1950.

 Halliday, J. L.: Epidemiology and the psychosomatic affections; study in social medicine, Lancet 2: 185 (Aug.) 1946.

 Halonen, P. I., and Jarvinen, K. A. J.: On the occurrence of neuropathic arthropathies in pernicious anaemia, Ann. Rheumat. Dis. 7: 152 (Sept.) 1948.

 Hamburger, H. J., and McNeil, C.: Epidemic myalgia or Bornholm disease in South India; review of 19 cases, Lancet 2: 784 (Nov.) 1947.

Hamburger, R. N.: Induction of lupus erythematosus ("L.E.") cell in vitro in peripheral blood, Yale J. Biol. and Med. 22: 407 (May) 1950.

 Hamilton, J. F.: Rheumatoid arthritis and its management, Mississippi Doctor 25: 169 (Oct.) 1947.

 Hammond, C. W., and Novak, M.: Relation of adrenal cortical steroids to antibody release, Proc. Soc. Exper. Biol. and Med. 74: 155 (May) 1950.

 Hammond, G., Hobelman, C. F., and Cady, J. B.: Spondylitis due to undulant fever; case report, Guthrie Clin. Bull. 16: 135 (Apr.) 1947.

- Hampton, O. P., Jr.: Observations on the management of suppurative arthritis of the knee joint, Am. J. Surg. 74: 631 (Nov.) 1947.
- 765. Hanisch, C. M., and Kleiger, B.: Experimental production of tendon sheaths; a preliminary report on the implantation of a flexible plastic in the tissues of rabbits and guinea pigs, Bull. Hosp. Joint Dis. 9: 22 (Apr.) 1948.
- 766. Hanlon, C. R.: DeQuervain's disease, Am. J. Surg. 77: 491 (Apr.) 1949.
- 767. Hanlon, C. R.: Nodular fibrositis, St. Luke's Hosp. Bull. 3: 94 (Nov.) 1948.
- Hanlon, C. R., and Estes, W. L.: Osteoarthritis aggravated by trauma, Am. J. Surg. 78: 556 (Nov.) 1949.
- Hanlon, C. R., and McLemore, R. A.: Clutton's joints, St. Luke's Hosp. Bull. 3: 53 (Aug.) 1948.
- Hansen, A. E.: Rheumatic recrudescences; diagnosis and prevention, J. Pediat. 28: 296 (Mar.) 1946.
- Hansen, A. E.: Consideration of management of child with rheumatic fever, New Orleans M. and S. J. 101: 264 (Dec.) 1948.
- 772. Hansen, G. A.: The origin of synovial mucin. Ehrlich's Mast Cell—a secretory element of the connective tissue, Ann. Rheumat. Dis. 9: 149 (June) 1950.
- Hansen, G. A.: Effect of the adrenocorticotropic hormone of the pituitary on mesenchymal tissues, Scandinav. J. Clin. and Lab. Invest. 2: 271, 1950.
- Hansson, K. G.: Physical medicine in the treatment of shoulder disabilities, Arch. Phys. Med. 31: 696 (Nov.) 1950.
- Hardgrove, M., Whittier, L., and Smith, E. R.: Rheumatic fever on the Isthmus of Panama, J. A. M. A. 130: 488 (Feb.) 1946.
- Harding, H. B.: Studies in the laboratory diagnosis of brucellosis; a critical review of literature, Quart. Bull., Northwestern Univ. M. School 22: 329, 1948.
- Harding, H. B.: Studies in the laboratory diagnosis of brucellosis; study of agglutination and brucellergen tests for brucellosis in asymptomatic population group, Quart. Bull., Northwestern Univ. M. School 23: 432, 1949.
- Hardy, J. B., and Hartmann, J. R.: Tuberculous dactylitis in childhood; prognosis, J. Pediat. 30: 146 (Feb.) 1947.
- Hardy, J. D., Riegel, C., and Erisman, E. P.: Experience with protein bound iodine (PBI); effect of ACTH and cortisone on thyroid function, Am. J. M. Sc. 219: 581 (May) 1950.
- 780. Hargraves, M. M.: Production in vitro of the L. E. cell phenomenon; use of normal bone marrow elements and blood plasma from patients with acute disseminated lupus erythematosus, Proc. Staff Meet., Mayo Clin. 24: 234 (Apr.) 1949.
- Hargraves, M. M., Richmond, H., and Morton, R.: Presentation of two bone marrow elements; the "tart" cell and "L. E." cell, Proc. Staff Meet., Mayo Clin. 23: 25 (Jan.) 1948.
- 782. Harkavy, J.: Allergic factors in gout, J. A. M. A. 139: 75, 1949.
- 783. Harkness, A. H.: Reiter's disease, Brit. M. J. 1: 72, and 1: 611, 1947.
- 784. Harkness, A. H.: Reiter's disease, Brit. J. Ven. Dis. 25: 185 (Dec.) 1949.
- Harmon, P. H.: Joint mobilizing operations on hip, knee, and shoulder for complications following trauma, Am. J. Surg. 74: 598 (Nov.) 1947.
- Harmon, P. H.: Results from treatment of sciatica due to lumbar disc protrusion, Am. J. Surg. 80: 829 (Nov.) 1950.
- 787. Harmon, P. H., Merryman, G. H., and Neuru, E. N.: Results from the treatment of 540 painful shoulders; a follow-up study of recoveries with special attention to tendon calcification, frozen shoulders and measures for the relief of pain, Permanente Found. M. Bull. 8: 60 (Apr.) 1950.
- 788. Harpuder, K.: Causalgia, Arch. Phys. Med. 27: 339 (June) 1946.
- 789. Harrell, G. T., and Horne, S. F.: Reaction to lepromin of patients with sarcoid or tu-

berculosis compared with that of patients in general hospitals, with discussion of mechanism of reaction, Am. J. Trop. Med. 25: 523 (Nov.) 1945.

 Harris, H. J.: Brucellosis; advances in diagnosis and treatment, J. A. M. A. 131: 1485 (Aug.) 1946.

 Harris, H. J.: Brucellosis; problems of diagnosis and treatment, Bull. New York Acad. Med. 22: 147 (Mar.) 1946.

Harris, H. W., and Meyers, S. G.: Salmonella suipestifer infection of the knee joint,
 J. Bone and Joint Surg. 30A: 217 (Jan.) 1948.

 Harris, Susanna, and Harris, T. N.: Effect of cortisone on reactions of hypersensitivity in laboratory animals, Proc. Soc. Exper. Biol. and Med. 74: 186 (May) 1950.

 Harris, Susanna, and Harris, T. N.: Serologic response to streptococcal hemolysin hyaluronidase in streptococcal and rheumatic infection, J. Clin. Investigation 29: 351 (Mar.) 1950.

795. Harris, T. N.: Treatment of acute rheumatic fever, Am. Pract. 1: 169 (Dec.) 1946.

 Harris, T. N.: Failure of massive salicylate therapy to suppress inflammatory reaction in rheumatic fever, Am. J. M. Sc. 213: 482 (Apr.) 1947.

 Harris, T. N.: Studies in the relation of hemolytic streptococcus to rheumatic fever; fractionation of hemolytic streptococcus by high speed centrifugation, J. Exper. Med. 87: 41 (Jan.) 1948.

 Harris, T. N.: Studies in the relation of hemolytic streptococcus to rheumatic fever; complement fixation versus streptococcal nucleoproteins with sera of patients with rheumatic fever and others, J. Exper. Med. 87: 57 (Jan.) 1948.

Harris, T. N.: Studies on the relation of the hemolytic streptococcus to rheumatic fever;
 review of serologic literature, Am. J. Dis. Child. 76: 411 (Oct.) 1948.

 Harris, T. N., and Friedman, S.: Relation of the hemolytic streptococcus to rheumatic fever; IV. effect of streptococcic spreading factor in rheumatic patients and others, Am. J. Dis. Child. 77: 561 (May) 1949.

 Harris, T. N., and Harris, S.: Turbidimetric measurement of streptococcal antihyaluronidase in the sera of patients with streptococcal infection and rheumatic fever, J. Immunol. 63: 249 (Nov.) 1949.

802. Harris, T. N., Harris, S., Dannenberg, A. M., and Hollander, J. L.: Streptococcal anti-hyaluronidase titers in the sera of patients with rheumatoid arthritis and glomerulo-nephritis. Ann. Int. Med. 32: 917 (May) 1950.

803. Harris, V. C. J.: Three cases of synovioma, Brit. M. J. 1: 447 (Mar.) 1948.

804. Harrison, M. H. M.: Familial outbreak of staphylococcal infection, Lancet 2: 727 (Nov.) 1948.

Harrison, R. G.: Relation of the adrenal cortex to arthritis, Lancet 1: 815 (June) 1946.
 Harrison, S. H.: Painful shoulder; significance of radiographic changes in upper end of humerus, J. Bone and Joint Surg. 31B: 418 (Aug.) 1949.

 Hart, F. D., Robinson, K. C., Allchin, F. M., and Maclagan, N. F.: Ankylosing spondylitis, Quart. J. Med. 18: 217 (July) 1949.

Hartung, E. F.: Toxic hepatitis during gold salts therapy; its effect on course of rheumatoid arthritis, M. Clin. North America 30: 553 (May) 1946.

 Hartz, P. H., and van der Sar, A.: Occurrence of rheumatic carditis in the native population of Curacao, Netherlands West Indies, Arch. Path. 41: 32 (Jan.) 1946.

 Harvey, A. M.: Introduction to series of papers on studies on ACTH and cortisone, Bull. Johns Hopkins Hosp. 87: 349 (Nov.) 1950.

811. Harvey, A. M., Howard, J. E., Winkenwerder, W. L., Bordley, J. F., Carey, R. C., and Kattus, A.: Observations on the effect of adrenocorticotropic hormone (ACTH) on disseminated lupus erythematosus, drug hypersensitivity reactions, and chronic bronchial asthma, Tr. Am. Clin. and Climatol. A. (1949) 61: 221, 1950.

812. Harvey, A. M., Tumulty, P. A., Bang, F. B., and Leftwich, W. B.: Epidemic myalgia, South. M. J. 41: 732 (Aug.) 1948.

- 813. Harvey, N. A.: Progressive coccidioidomycosis; report of case, Ann. Int. Med. 28: 651 (Mar.) 1948.
- 814. Haserick, J. R.: Blood factor in acute disseminated lupus erythematosus, Arch. Dermat. and Syph. 61: 889 (June) 1950.
- Haserick, J. R., and Bortz, D. W.: New diagnostic test for acute disseminated lupus erythematosus, Cleveland Clin. Quart. 16: 158 (July) 1949.
- 816. Haserick, J. R., and Bortz, D. W.: Normal bone marrow inclusion phenomena induced by lupus erythematosus plasma, J. Invest. Dermat. 13: 47 (Aug.) 1949.
- 817. Haserick, J. R., and Lewis, L. A.: Blood factor in acute disseminated lupus erythematosus; induction of specific antibodies against L. E. factor, Blood 5: 718 (Aug.) 1950.
- Haserick, J. R., Lewis, L. A., and Bortz, D. W.: Blood factor in acute disseminated lupus erythematosus; determination of gamma globulin as specific plasma fraction, Am. J. M. Sc. 219: 660 (June) 1950.
- 819. Haserick, J. R., and Sundberg, R. D.: Bone marrow as diagnostic aid in acute disseminated lupus erythematosus; report on Hargraves' "L. E." cell, J. Invest. Dermat. 11: 209 (Sept.) 1948.
- 820. Hauser, H.: Pulmonary sarcoidosis, J. Oklahoma M. A. 39: 395 (Oct.) 1946.
- Hawn, C. V., and Janeway, C. A.: Histological and serological sequences in experimental hypersensitivity, J. Exper. Med. 85: 571, 1947.
- 822. Hay, B. M.: Two cases of osteochondritis dissecans affecting several joints, J. Bone and Joint Surg. 32B: 361 (Aug.) 1950.
- 823. Hayes, M. A., and Reed, T. G.: Factors influencing measurement of hyaluronidase activity by dermal spread of an indicator, Proc. Soc. Exper. Biol. and Med. 75: 357, 1050
- 824. Hayes, M. A., Reed, T. G., and Baker, B. L.: Dermal spreading of hyaluronidase as influenced by prolonged local treatment with adrenal cortical extract, Proc. Soc. Exper. Biol. and Med. 75: 361, 1950.
- 825. Haynes, D. M., and Hess, W. I.: Cutaneous test with coccidioidin; review of literature and report of a series in Texas, J. Lab. and Clin. Med. 31: 1317 (Dec.) 1946.
- 826. Haynes, W. G.: Surgical treatment of protruded intervertebral cervical disc, South. Surgeon 16: 496 (May) 1950.
- 827. Haythorn, S. R.: Pathological changes found in material removed at operation in Legg-Calve-Perthes disease, J. Bone and Joint Surg. 31A: 599 (July) 1949.
- Heald, C. B.: Common forms of arthritis and rheumatism, New Zealand M. J. 46: 497 (Dec.) 1947.
- Heald, C. B., Lush, B., and Buchan, J. F.: Perspex splint for ulnar-deviation of the fingers, Lancet 1: 396 (Mar.) 1949.
- 830. Hechter, O.: Reconstitution of dermal barrier to fluid diffusion following administration of hyaluronidase, Proc. Soc. Exper. Biol. and Med. 67: 343 (Mar.) 1948.
- Hecker, H.: Metastatic calcification and renal failure following Ertron therapy in an aged arthritic, Rhode Island M. J. 33: 21 (Jan.) 1950.
- Hedlund, P., and Löfström, G.: Serologic studies in experimentally produced polyarthritis, Acta med. Scandinav. 124: 535, 1946.
- 833. Heilbrun, N., and Kuhn, W. G., Jr.: Erosive bone lesions and soft-tissue ossifications associated with spinal cord injuries (paraplegia), Radiology 48: 579 (June) 1947.
- Heilbrunn, I. B., and Cain, A. R.: Mild histoplasmosis clinically resembling atypical pneumonia and accompanied by erythema nodosum and arthritis, J. Missouri M. A. 47: 503 (July) 1950.
- 835. Heilman, F. R.: The effect of combined treatment with aureomycin and dihydrostreptomycin on brucella infections in mice, Proc. Staff Meet., Mayo Clin. 24: 133 (Mar.) 1949.
- 836. Heinrich, M. R., and Wilson, D. W.: Biosynthesis of nucleic acid components studied with C¹⁴; purines and pyrimidines in rat, J. Biol. Chem. 186: 447 (Oct.) 1950.

837. Helfet, A. J.: Consideration of recent surgery of osteoarthritis of hip joint, South African M. J. 24: 637 (Aug.) 1950.

838. Hellebrandt, F. A., Duvall, E. N., and Moore, M. L.: Measurement of joint motion: reliability of goniometry, Physiotherapy Rev. 29: 302 (July) 1949.

839. Hellebrandt, F. A., Houtz, S. J., and Kelso, L. E. A.: New devices for disability evaluation; the grip ergograph, Arch. Phys. Med. 31: 207 (Apr.) 1950.

840. Heller, G., Jacobson, A. S., and Kolodny, M. H.: Modification of hemagglutination test for rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 72: 316 (Nov.) 1949.

841. Hellman, L.: Production of acute gouty arthritis by adrenocorticotropin, Science 109: 280 (Mar.) 1949.

842. Hellman, L.: The relation of life stress to arthritis, A. Research Nerv. and Ment. Dis. Proc. (1949) 29: 412, 1950.

843. Hemphill, J. E., and Shull, J. R.: Vacuum technique for the simple demonstration of rupture of the medial meniscus of the knee, North Carolina M. J. 8: 568 (Sept.) 1947.

844. Hench, P. S.: Therapeutic "Information Please"; arthritis, J. A. M. A. 132: 974 (Dec.) 1946.

845. Hench, P. S.: Gold salts for rheumatoid arthritis [Editorial], Ann. Int. Med. 26: 618 (Apr.) 1947.

846. Hench, P. S.: Differentiation between "psychogenic rheumatism" and true rheumatic disease, Postgrad. Med. 1: 460 (June) 1947.

847. Hench, P. S.: Consultation and case-analysis, Arizona Med. 4: 62 (July) 1947.

848. Hench, P. S.: The potential reversibility of rheumatoid arthritis, Proc. Staff Meet., Mayo Clin. 24: 167 (Mar.) 1949; also, Ann. Rheumat. Dis. 8: 90 (June) 1949.

849. Hench, P. S.: Cortisone and ACTH in clinical medicine, Proc. Staff Meet., Mayo Clin. 25: 474 (Aug.) 1950.

850. Hench, P. S.: The present status of cortisone and ACTH in general medicine, Proc. Roy. Soc. Med. 43: 769 (Oct.) 1950 (Section Exp. Med. & Therapeut. 27, 1950).

851. Hench, P. S.: Discussion, Proc. Amer. Rheumat. A. Meeting, San Francisco, June, 1950, Ann. Rheumat. Dis. 9: 397 (Dec.) 1950.

852. Hench, P. S., and Boland, E. W.: Management of chronic arthritis and other rheumatic diseases among soldiers of the United States Army, Ann. Rheumat. Dis. 5: 106 (June) 1946.

853. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis, Proc. Staff Meet., Mayo Clin. 24: 181 (Apr.) 1949.

854. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: Effects of cortisone acetate and pituitary ACTH on rheumatoid arthritis, rheumatic fever and certain other conditions; a study in clinical physiology, Arch. Int. Med. 85: 545 (Apr.) 1950.

855. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: The effect of a hormone of the adrenal cortex, cortisone (17-hydroxy-11-dehydrocorticosterone: compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis and acute rheumatic fever, preliminary report, Tr. A. Am. Physicians 62: 64, 1949.

856. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: The antirheumatic effects of cortisone and pituitary ACTH, Tr. and Stud., Coll. Physicians, Philadel-

phia 18: 95 (Dec.) 1950.

857. Hench, P. S., Slocumb, C. H., Polley, H. F., and Kendall, E. C.: Effect of cortisone and pituitary adrenocorticotropic hormone (ACTH) on rheumatic diseases, J. A. M. A. 144: 1327 (Dec.) 1950.

858. Hench, P. S., Slocumb, C. H., and Polley, H. F.: Rheumatoid spondylitis; questions and answers, M. Clin. North America 31: 879 (July) 1947.

859. Hench, P. S., Slocumb, C. H., Barnes, A. R., Smith, H. L., Polley, H. F., and r.endall, E. C.: The effects of the adrenal cortical hormone 17-hydroxy-11-dehydrocorticosterone (compound E) on the acute phase of rheumatic fever; preliminary report, Proc. Staff Meet., Mayo Clin. 24: 277 (May) 1949.

- 860. Henderson, E., Gray, J. W., Weinberg, M., Merrick, E. Z., and Seneca, H.: Some preliminary observations on the treatment of rheumatoid arthritis with cortisone plus insulin, J. Clin. Endocrinol. 10: 800 (July) 1950.
- Hendryson, I. E.: Bursitis in region of fibular collateral ligament, J. Bone and Joint Surg. 28: 446 (July) 1946.
- 862. Henske, J. A.: The care of the child with rheumatic heart disease, Nebraska M. J. 32: 223 (June) 1947.
- 863. Hepburn, H. H.: Protruded intervertebral disc, Canad. M. A. J. 57: 273 (Sept.) 1947.
- 864. Hepburn, R. H.: Reiter's syndrome treated successfully with dihydrostreptomycin, J. Urol. 64: 413 (Aug.) 1950.
- Herbert, J. J.: Vertebral osteotomy; technic, indications and results, J. Bone and Joint Surg. 20A: 680 (July) 1948.
- Hermanson, R. H.: Bilateral osteochondritis dissecans of knee, Radiology 47: 349 (Oct.) 1946.
- 867. Hermodsson, I.: On problem of trauma and aseptic osteonecrosis, Acta radiol. 28: 257, 1947.
- Hernaman-Johnson, F.: Thorium X in spondylitis and chronic rheumatism, Rheumatism
 21 (July-Sept.) 1946.
- 869. Hernaman-Johnson, F.: X-ray treatment in osteoarthritis, Rheumatism 5: 44 (Apr.)
- 870. Herrell, W. E., and Barber, T. E.: A new method for treatment of brucellosis, J. A. M. A. 144; 519 (Oct.) 1950.
- 871. Herrell, W. E., and Nichols, D. R.: The combined use of streptomycin and sulfadiazine in the treatment of brucellosis, M. Clin. North America 33: 1079 (July) 1949.
- 872. Hersh, A. H., Stecher, R. M., Solomon, W. M., Wolpaw, R., and Hauser, H.: Heredity in ankylosing spondylitis; a study of 50 families, Am. J. Human Genet. 2: 391 (Dec.) 1050
- 873. Hersh, J.: Pneumococcal arthritis, Am. J. Surg. 72: 748 (Nov.) 1946.
- 874. Herson, R. N.: Reiter's disease, Brit. M. J. 2: 275, 1946.
- 875. Herz, R.: Herniation of subfascial fat as cause of low back pain; results of surgical treatment in 31 cases, J. Internat. Coll. Surgeons 9: 339 (May-June) 1946.
- 876. Herz, R.: Herniation of subfascial fat as cause of low back pain; report of 37 cases treated surgically, Ann. Rheumat. Dis. 5: 201 (Dec.) 1946.
- Heyman, A., Wall, M. J., and Beeson, P. B.: Effect of sulfonamide therapy on the persistence of the virus of lymphogranuloma venereum in buboes, Am. J. Syph., Gonor. and Ven. Dis. 31: 81 (Jan.) 1947.
- 878. Higbee, D.: Brief review of rheumatic fever; role of tonsillitis in its etiology, Ann. Otol., Rhin. and Laryng. 55: 227 (June) 1946.
- Higgins, T. T., Browne, D., and Bodian, M.: Penicillin-treated series of cases of osteomyelitis in childhood, Brit. M. J. 1: 757 (May) 1947.
- Highberger, J. H., Gross, J., and Schmitt, F. O.: Electron microscope observations of certain fibrous structures obtained from connective tissue extracts, J. Am. Chem. Soc. 72: 3321, 1950.
- 881. Higley, C. S.: Recent advances in the control of rheumatic fever, Postgrad. Med. 2: 75 (Aug.) 1947.
- 882. Hilker, A. W.: The shoulder-hand syndrome; a complication of coronary artery disease, Ann. Int. Med. 31: 303 (Aug.) 1949.
- 883. Hill, D. F., and Holbrook, W. P.: Prevention and treatment of deformities in rheumatoid arthritis, J. A. M. A. 142: 718 (Mar.) 1950.
- Hill, K. R., Findlay, G. M., and Macpherson, A.: Treatment of yaws with penicillin, Lancet 2: 522 (Oct.) 1946.

885. Hill, L. C.: Review of gout, 1939-1946, Ann. Rheumat. Dis. 5: 171 (Sept.) 1946.

 Hill, S. R., Jr., Reiss, R. S., Forsham, P. H., and Thorn, G. W.: Effect of adrenocorticotropin and cortisone on thyroid function: thyroid-adrenocortical interrelationships, J. Clin. Endocrinol. 10: 1375 (Nov.) 1950.

887. Hill, W. R., and Kinney, T. D.: Cutaneous lesions in acute meningococcemia; clinical

and pathologic study, J. A. M. A. 134: 513 (June) 1947.

888. Hinchey, J. J., Hines, E. A., Jr., and Ghormley, R. K.: Osteoporosis occurring during potassium thiocyanate therapy for hypertensive disease, Proc. Staff Meet., Mayo Clin. 22: 275 (July) 1947.

 Hirsch, E. F., and Riley, J. W.: Traumatic proliferations of fibrocartilage with ossification in genesis of spondylitis deformans and myositis ossificans, Arch. Path. 44: 445 (Nov.) 1947.

 Hirsh, H. L., Feffer, H. L., and Dowling, H. F.: Treatment of bacterial arthritis with penicillin, New England J. Med. 234: 853 (June) 1946.

 Hirsh, H. L., Feffer, H. L., and O'Neil, C. B.: Study of diffusion of penicillin across serous membranes of joint cavities, J. Lab. and Clin. Med. 31: 535 (May) 1946.

Hirschboeck, J. S.: Hematologic effects of splenectomy in Still-Chauffard-Felty syndrome; report of 2 cases, Blood 1: 247 (May) 1946.

 Hitchcock, H. H., and Bechtol, C. O.: Observations on the role of the tendon of the long head of the biceps brachii in its causation, J. Bone and Joint Surg. 30A: 263 (Apr.) 1948.

894. Hittner, V. J.: Episacroiliac lipomas, Am. J. Surg. 78: 382 (Sept.) 1949.

895. Hodas, J. H., Brandon, H., and Maloney, J. F.: Treatment of rheumatic diseases with glucuronic acid; a preliminary report, Journal Lancet 69: 385 (Nov.) 1949.

 Hodges, F. M., and Boyer, R. A.: Roentgen therapy of bursitis, Virginia M. Monthly 75: 547 (Nov.) 1948.

 Hoefer, P. F. A., and Glaser, G. H.: Effects of pituitary adrenocorticotropic hormone (ACTH) therapy. Electroencephalographic and neuropsychiatric changes in 15 patients, J. A. M. A. 143: 620 (June) 1950.

 Hoen, T. I., Anderson, R. K., and Clare, F. B.: Symposium on neurosurgery; lesions of intervertebral disks, S. Clin. North America 28: 456 (Apr.) 1948.

 Hofer, J. W.: Oral penicillin for children with rheumatic fever, J. Pediat. 35: 135 (Aug.) 1949.

900. Hoffman, H. L.: Pain in the arm; a review, Ann. Rheumat. Dis. 7: 9 (Mar.) 1948.

901. Hoffman, H. L.: Sciatic pain, Post-Grad. M. J. 23: 151 (Mar.) 1947.

 Hoffman, H. L., and Elliott, F. A.: Discussion on neurological aspects of rheumatic diseases, Proc. Roy. Soc. Med. 42: 575 (Aug.) 1949.

 Hoffman, W. S., and Nobe, C.: The influence of urinary pH on renal excretion of salicyl derivatives during aspirin therapy, J. Lab. and Clin. Med. 35: 237 (Feb.) 1950

904. Hoffman, W. S., Pomeranc, M., Volini, I. F., and Nobe, C.: Treatment of acute rheumatic fever with aspirin with special reference to the biochemical changes, Am. J. Med. 6: 433 (Apr.) 1949.

 Höjer, J. A.: Organization of rheumatism research and treatment in Sweden, Ann. Rheumat. Dis. 5: 183 (Dec.) 1946.

 Holbrook, W. P.: Prevention of rheumatic fever, Chicago M. Soc. Bull. 51: 158 (Sept.) 1948.

 Holbrook, W. P., Hill, D. F., Stephens, C. A. L., and Kent, L. J.: Effects of ACTH and cortisone on rheumatoid arthritis, Arizona Med. 7: 43 (July) 1950.

 Holbrook, W. P., Hill, D. F., Stevens, A. L., Kent, L., and McCarthy, E.: Treatment of rheumatoid arthritis, Postgrad. M. 5: 399 (May) 1949.

Hollander, J. L.: Diagnosis and treatment of Reiter's syndrome, M. Clin. North America 30: 716 (May) 1946.

- Hollander, J. L.: Experiences with ACTH and cortisone, Philadelphia Med. 45: 1205 (Apr.) 1950.
- Hollander, J. L., and Horvath, S. M.: The influence of physical therapy procedures on the intra-articular temperature of normal and arthritic subjects, Am. J. M. Sc. 218: 543 (Nov.) 1949.
- Holmes, H. H., Bauman, E., and Ragan, C.: Symptomatic arthritis due to hypertrophic pulmonary osteoarthropathy in pulmonary neoplastic disease; a report of 7 cases, Ann. Rheumat. Dis. 9: 169 (June) 1950.
- 913. Holmes, J. M.: Case of acute dermatomyositis, Brit. M. J. 2: 511 (Sept.) 1948.
- 914. Holmes, J. M., and Sworn, B. R.: Lumbo-sacral root pain, Brit. M. J. 1: 946 (June) 1946.
- 915. Holmes, T. H., and Wolff, H. G.: Life situations, emotions and backaches, A. Research Nerv. and Ment. Dis. Proc. (1949) 29: 750, 1950.
- Holoubek, J. E., and Holoubek, A. B.: Heart disease in the South; statistical survey of 117 deaths due to rheumatic heart disease, Am. Heart J. 34: 709 (Nov.) 1947.
- 917. Holt, J. F.: Ehlers-Danlos syndrome, Am. J. Roentgenol. 55: 420 (Apr.) 1946.
- 918. Holt, J. F., and Owens, W. I.: The osseous lesions of sarcoidosis, Radiology 53: 11 (July) 1949.
- Hoover, M. J., Jr.: Treatment of tuberculous psoas abscess, South. Surgeon 16: 729 (Aug.) 1950.
- 920. Hopkins, F.: Do bony spurs cause pain? Virginia M. Monthly 74: 179 (Apr.) 1947.
- 921. Hopkins, J. H. S.: Bornholm disease, Brit. M. J. 1: 1230 (May) 1950.
- Hopkins, J. J., and Richmond, J. B.: Palindromic rheumatism, Ann. Int. Med. 26: 454 (Mar.) 1947.
- Hopps, H. C., and Wissler, R. W.: Experimental production of generalized arteritis and periarteritis (periarteritis nodosa), J. Lab. and Clin. Med. 31: 939 (Sept.) 1946.
- Horne, S. F., Curtis, A. C., and Kahn, E. A.: Splanchnicectomy for hypertension in lupus erythematosus and periarteritis nodosa, Ann. Int. Med. 32: 1202 (June) 1950.
- Horner, J. L.: Premature calcification of the costal cartilages; its frequent association with psychoneuroses and possible endocrine imbalance, J. Lab. and Clin. Med. 33: 1621 (Dec.) 1948.
- Horner, J. L.: Premature calcification of the costal cartilages; its frequent association with symptoms of non-organic origin, Am. J. M. Sc. 218: 186 (Aug.) 1949.
- Horwitz, H., and Joseph, N. R.: Prolonged observation on a group of arthritic patients, Indust. Med. 15: 100 (Feb.) 1946.
- Horwitz, M.: Syphilitic spondylitis with a report of 2 cases, Ann. Rheumat. Dis. 7: 200 (Dec.) 1948.
- Horwitz, M.: Muscle lesions in rheumatoid arthritis, Ann. Rheumat. Dis. 8: 258 (Dec.) 1949.
- Horwitz, M.: The subcutaneous nodules of rheumatoid arthritis with lipoid deposition, Ann. Rheumat. Dis. 8: 181 (Sept.) 1949.
- Horwitz, T.: Bone and cartilage debris in the synovial membrane; its significance in the early diagnosis of neuroarthropathy, J. Bone and Joint Surg. 30A: 579 (July) 1948.
- 932. Horwitz, T.: Degenerative osteoarthritis of the hip joint; survey of degenerative arthritis secondary to aseptic necrosis of the femoral head, Arch. Surg. 58: 251 (Mar.) 1040
- Horwitz, T., and Lambert, R. G.: Patellectomy in military service; report of 19 cases, Surg., Gynec. and Obst. 82: 423 (Apr.) 1946.
- Houston, J., Whittington, R. B., Cowan, I. C., and Harkness, J.: The plasma viscosity in pulmonary tuberculosis and rheumatic diseases, J. Clin. Investigation 28: 752 (July) 1949.
- 935. Howard, C.: Traumatic ossifying myositis, U. S. Nav. M. Bull. 46: 724 (May) 1946.

- Howard, J. E., Harvey, A. McG., Carey, R. A., and Winkenwerder, W. L.: Effects of pituitary adrenocorticotropic hormone (ACTH) on the hypersensitive state, J. A. M. A. 144: 1347 (Dec.) 1950.
- Howard, R. P., Venning, E. H., and Fisk, G. H.: Studies of adrenocortical and hypophyseal function and the effects thereon of testosterone and pregnenolone therapy, Canad. M. A. J. 63: 340, 1950.
- Howell, T. H.: Treatment of fibrositis with adrenaline, ephedrine, and belladonna creams, Lancet 2: 395 (Sept.) 1950.
- Howell, T. H.: Relief of pain in rheumatoid arthritis with tetraethylammonium bromide, Lancet 1: 204 (Feb.) 1950.
- 940. Howell, T. H.: A simple treatment for fibrositis, M. Press 223: 514 (May) 1950.
- 941. Howes, E. L., Plotz, C. M., Blunt, J. W., Jr., and Ragan, C.: Retardation of wound healing by cortisone, Surgery 28: 177 (Aug.) 1950.
- 942. Howles, J. K.: Sarcoidosis in Negro, South. M. J. 43: 633 (July) 1950.
- Hucherson, D. C., and Denman, F. R.: Non-infectious iliopectineal bursitis, Am. J. Surg. 72: 576 (Oct.) 1946.
- Hucherson, D. C., and Denman, F. R.: Painful motions of the thumb; stenosing tenosynovitis of the flexor pollicis longus, West. J. Surg. 56: 370 (June) 1948.
- 945. Hueper, W. C.: Cinchophen (atophan), a critical review, Medicine 27: 43 (Feb.) 1948.
- Hughes, E. S. R.: Osgood-Schlatter's disease, Surg., Gynec. and Obst. 86: 323 (Mar.) 1948.
- Hughes, E. S. R.: Acute deposition of calcium near elbow, J. Bone and Joint Surg. 32B: 30 (Feb.) 1950.
- Hume, D. M.: The role of the hypothalamus in the pituitary-adrenal cortical response to stress, J. Clin. Investigation 28: 790, 1949.
- 949. Humphrey, J. H.: The nature of antistreptolysin "S" in the sera of man and of other species: antistreptolysin titres in normal and diseased states, Brit. J. Exper. Path. 30: 345, 1949.
- Humphrey, J. H.: The nature of antistreptolysin S in the sera of man and of other species. The lipoprotein properties of antistreptolysin S, Brit. J. Exper. Path. 30: 365, 1949.
- Humphreys, E. M.: Cardiac lesions of acute disseminated lupus erythematosus, Ann. Int. Med. 28: 12 (Jan.) 1948.
- 952. Humphreys, F. A., Campbell, A. G., Driver, M. W., and Hatton, G. N.: Rat bite fever, Canad. J. Pub. Health 41: 66 (Feb.) 1950.
- 953. Huntington, R. W., Jr., Ryan, R. D., Butt, H. R., Griffith, G. C., Montgomery, H., Solley, R. F., and Leake, W. H.: Studies in rheumatic fever; absorption of salicylates, Ann. Int. Med. 24: 1029 (June) 1946.
- Hurt, S. P.; Joint measurement, Am. J. Occup. Therapy 1: 209 (Aug.) 1947; 281 (Oct.) 1947.
- Hyde, J. S., and Richmond, J. B.: Vitamin D intoxication in a child with rheumatoid arthritis, Am. J. Dis. Child. 80: 379 (Sept.) 1950.
- Hyde, L., and Hyde, B.: Toxicity of large doses of vitamin D (Ertron), Ann. Int. Med. 27: 617 (Oct.) 1947.
- Ingle, D. J.: Biologic properties of cortisone; a review, J. Clin. Endocrinology 10: 1312 (Oct.) 1950.
- Inman, V. T., and Saunders, J. B. de C. M.: Anatomico-physiological aspects of injuries to the intervertebral disc, J. Bone and Joint Surg. 29: 461, 1947.
- 959. Irgang, S.: Sarcoid of Boeck in Negro, Arch. Dermat. and Syph. 56: 659 (Nov.) 1947.
- 960. Ishmael, W. K.: Rheumatism in aged, Geriatrics 3: 217 (July-Aug.) 1948.
- 961. Ishmael, W. K.: Degenerative arthritis, Am. Pract. 4: 97 (Oct.) 1949.
- 962. Ishmael, W. K., Hellbaum, A., Kuhn, J. F., and Duffy, M.: The effects of certain

- steroid compounds on various manifestations of rheumatoid arthritis; a preliminary report, J. Oklahoma M. A. 42: 434 (Oct.) 1949.
- Ishmael, W. K., and Stacy, J. R.: Use of dolophine (dimethylamino heptanone-methadon) in control of pain in bone and joint disorders, J. Oklahoma M. A. 40: 454 (Nov.) 1947.
- 964. Isserlin, B.: Joint debridement for osteoarthritis of the knee, J. Bone and Joint Surg. 32B: 302 (Aug.) 1950.
- Ivins, J. C.: Streptomycin and extrapulmonary tuberculosis; streptomycin in treatment of bone-joint tuberculosis, sinuses, and fistulae, Nat. Tuberc. A. Tr. (1949) 45: 108, 1950.
- 966. Jackson, H.: The association between certain anatomical facts, normal and morbid, and symptomatology of intervertebral disc protrusions in the lumbar region, Ann. Roy. Coll. Surgeons, England 2: 273 (June) 1948.
- Jackson, R. L.: Heart disease in children in a rural Iowa county—particularly in relation to rheumatic fever, J. Pediat. 29: 647 (Nov.) 1946.
- Jackson, R. L.: Treatment of acute rheumatic fever and prevention of recurrences,
 J. A. M. A. 141: 439 (Oct.) 1949.
- Jackson, R. L., Kelly, H. G., Rohret, C. H., and Duane, J. M.: Rheumatic fever recurrences in children without sulfonamide prophylaxis; evaluation of environmental factors, J. Pediat. 31: 390 (Oct.) 1947.
- 970. Jackson, W. P. U.: Syndrome known as "Reiter's disease" (triad of polyarthritis, urethritis, and conjunctivitis), Brit. M. J. 2: 197, 1946.
- 971. Jackson, W. P. U.: Significance of clubbing of the fingers, Brit. M. J. 1: 216 (Feb.) 1949.
- Jacobs, J. E.: The thoracolumbar syndrome as a common cause of backache, North Carolina M. J. 9: 122 (Mar.) 1948.
- 973. Jacobs, J. E., and Lee, F. W.: Hemangioma of the knee joint, J. Bone and Joint Surg. 31A: 831 (Oct.) 1949.
- Jacobsson, E.: Rheumatic fever with chorea minor; clinical study with special reference to prognosis, Acta paediat. (suppl. 7) 33: 1, 1946.
- Jager, B. V., and Alway, R.: Treatment of acute rheumatic fever with large doses of sodium salicylate, with special reference to dose management and toxic manifestations, Am. J. M. Sc. 211: 273 (Mar.) 1946.
- Jailer, J. W., and Knowlton, A. I.: Simulated adreno-cortical activity during pregnancy in an addisonian patient, J. Clin. Investigation 29: 1430 (Nov.) 1950.
- James, E. S.: Protruded cervical intervertebral discs—cause of brachial neuritis, Canad. M. A. J. 55: 139 (Aug.) 1946.
- James, U.: Collapsed intervertebral discs following lumbar puncture, Proc. Roy. Soc. Med. 39: 134 (Jan.) 1946.
- James, W. E., Little, R. C., and Shumway, N. P.: Effect of desoxycorticosterone and ascorbic acid on rheumatoid arthritis, Am. J. M. Sc. 220: 490 (Nov.) 1950.
- 980. Jamieson, W. M., and Prinsley, D. M.: Bornholm disease in tropics, Brit. M. J. 2: 47 (July) 1947.
- Jampol, H.: Exercise treatment for frozen shoulder, Physiotherapy Rev. 30: 221 (June) 1950.
- Järvinen, K. A. J.: A study of the interrelations of rheumatoid arthritis and diabetes mellitus, Ann. Rheumat. Dis. 9: 226 (Sept.) 1950.
- 983. Jawetz, E., and Hook, E.: Differential sheep cell agglutination test in rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 70: 650, 1949.
- 984. Jaworski, A. A., Farley, J. E., Jr., Barrett, J., and Jaworski, R. A.: Relation of hyaluronidase to salicylates and rheumatic fever, J. Pediat. 37: 697 (Nov.) 1950.
- 985. Jeanloz, R.: Hotchkiss reaction and structure of polysaccharides, Science 3: 289 (Mar.) 1950.

- Jeanloz, R. W., and Forchielli, E.: Studies on hyaluronic acid and related substances; preparation of hyaluronic acid and derivatives from human umbilical cord, J. Biol. Chem. 186: 495 (Oct.) 1950.
- Jefferson, N. C., Palmer, J. M., and Phillips, C. W.: Tuberculosis of the greater trochanter and its bursa; treatment with streptomycin and surgery, J. Internat. Coll. Surgeons 13: 361 (Apr.) 1950.
- Jellison, W. L., Eneboe, P. L., Parker, R. R., and Hughes, L. E.: Rat bite fever in Montana, Pub. Health Rep. 64: 1661 (Dec.) 1949.
- 989. Jennings, G. H.: Amyloidosis in rheumatoid arthritis, Brit. M. J. 1: 753 (Apr.) 1950.
- Jensen, C. R.: Nonsuppurative poststreptococcic (rheumatic) pneumonitis; pathologic anatomy and clinical differentiation from primary atypical pneumonia, Arch. Int. Med. 77: 237 (Mar.) 1946.
- Jensen, W. P.: Symposium on psychosomatic medicine; psychosomatic disorders of muscles, bones and joints, Nebraska M. J. 35: 179 (June) 1950.
- Jespersen, K.: Cervical sympathetic block in periarthrosis of shoulder joint with secondary reflex dystrophy, Ann. Rheumat. Dis. 8: 220 (Sept.) 1949.
- 993. Jespersen, K.: Fibrositis of muscles, Ann. Rheumat. Dis. 9: 66 (Mar.) 1950.
- Jespersen, K.: The effect of ACTH in a case of humeroscapular periarthritis, Scandinav. J. Clin. and Lab. Invest. 2: 284, 1950.
- 995. Johnson, A., Shapiro, L. B., and Alexander, F.: Preliminary report on psychosomatic study of rheumatoid arthritis, Psychosom. Med. 9: 295 (Sept.-Oct.) 1947.
- Johnson, J. B., and Mazique, E. C.: Disseminated lupus erythematosus unsuccessfully treated with penicillin, roentgen-ray castration and serum albumin, Ann. Int. Med. 25: 859 (Nov.) 1946.
- Johnson, R. M., and Hecht, H. H.: Palmar erythema—its relationship to protein deficiency, Am. J. M. Sc. 211: 79 (Jan.) 1946.
- Johnson, S. A. M., and Falls, H. F.: Ehlers-Danlos syndrome; a clinical and genetic study, Arch. Dermat. and Syph. 60: 82 (July) 1949.
- Jonas, A. F.: Surgical relief of pain in shoulder and upper extremity, Pennsylvania M. J. 51: 1403 (Sept.) 1948.
- 1000. Jonas, A. F., Jr., and Rise, W. S.: Bilateral cervical ribs associated with neuropathic joints, Arch. Surg. 56: 224 (Feb.) 1948.
- 1001. Jones, E. S.: Hyaluronidase activity in skin, rheumatic disease, and salicylates, Ann. Rheumat. Dis. 9: 137 (June) 1950.
- 1002. Jones, F. W.: Classical gout (syndrome connected with disturbance of vasomotor nerves); Heberden oration, Brit. M. J. 1: 561 (Mar.) 1950.
- 1003. Jones, G. B.: Surgical diagnosis of acute injuries of the knee joint, S. Clin. North America 26: 402 (Apr.) 1946.
- 1004. Jones, G. B.: The behavior of penicillin in synovial cavities, J. Bone and Joint Surg. 30B: 106, 1948.
- 1005. Jones, G. B.: Painful shoulder; calcification of supraspinatus tendon, J. Bone and Joint Surg. 31B: 433 (Aug.) 1949.
- 1006. Jones, H. T.: Low back pain from the orthopedic standpoint, California Med. 68: 57 (Feb.) 1948.
- 1007. Jones, I. S., and Meyer, K.: Inhibition of vascularization of the rabbit cornea by local application of cortisone, Proc. Soc. Exper. Biol. and Med. 74: 102 (May) 1950.
- 1008. Jones, R. H., Jr., and Moore, W. W.: Purpuric manifestations of rheumatic fever and acute glomerulonephritis, Am. Heart J. 32: 529 (Oct.) 1946.
- 1009. Jones, T. D.: Rheumatic fever, Tr. A. Life Insur. M. Dir. America (1946) 30: 9, 1947.
- 1011. Jonsson, E.: Arthralgia due to nervous causes, Acta med. Scandinav. 123: 529, 1946.
- 1012. Jonsson, E., and Berglund, K.: Trauma and rheumatoid arthritis, Acta med. Scandinav. 135: 255, 1949.

- 1013. Jordan, C. F., and Borts, I. H.: Occurrence of Brucella melitensis in Iowa, J. A. M. A. 130: 72 (Jan.) 1946.
- 1014. Joseph, N. R., Reed, C. I., and Homburger, E.: In vivo study of pH of synovial fluid in dogs, Am. J. Physiol. 146: 1 (Apr.) 1946.
- 1015. Joseph, N. R., Reed, C. I., Steck, I. E., Folk, F., and Kaplan, E.: An electrochemical study of the synovialis in dogs, Am. J. Physiol. 153: 364 (May) 1948.
- 1016. Jowett, A. E.: Opaque arthrography of the knee joint, Ann. Rheumat. Dis. 8: 149 (June) 1949.
- 1017. Judovich, B. D.: Scalenus anticus syndrome, New York State J. Med. 48: 2382 (Nov.) 1948.
- 1018. Judovich, B. D., Bates, W., and Jacobs, M. S.: Possible mechanism of postcoronary shoulder pain, Am. J. Surg. 78: 216 (Aug.) 1949.
- 1019. Judovich, B., and Nobel, G.: Relief of pain in osteoarthritis of hip joint, Am. J. Surg. 72: 72 (July) 1946.
- 1020. Kabat, H., and Jones, C. W.: Studies on neuromuscular dysfunction; neostigmine therapy of acute and chronic backache, Arch. Phys. Med. 27: 208 (Apr.) 1946.
- 1021. Kagan, B. M., and Mirman, B.: Sydenham's chorea, syndrome for differential diagnosis, J. Pediat. 31: 322 (Sept.) 1947.
- 1022. Kagan, B. M., Rosner, D. C., and Rosenblum, P.: Chorea (Sydenham); a study of 58 additional patients, Am. J. Dis. Child. 78: 306 (Sept.) 1949.
- 1023. Kaiser, R. A.: Obturator neurectomy for coxalgia; an anatomical study of the obturator and the accessory obturator nerves, J. Bone and Joint Surg. 31A: 815 (Oct.) 1949.
- 1024. Kalbak, K.: Agglutination of hemolytic streptococci (group A) in serum from patients with rheumatoid arthritis, Ann. Rheumat. Dis. 6: 230 (Dec.) 1947.
- 1025. Kalz, F.: Syphilitic juxta-articular nodes, Arch. Dermat. and Syph. 60: 426 (Sept.) 1949.
- 1026. Kammerling, E., Lewis, G. N., and Ehrlich, L.: Recurrent post-infarctional shoulder-hand syndrome; report of a case with unusual clinical evolution, New England J. Med. 242: 701 (May) 1950.
- 1027. Kampmeier, R. H.: Vascular diseases due to hypersensitivity: so-called diffuse collagen disease, Am. Pract. and Digest Treat. 1: 113 (Feb.) 1950.
- 1028. Kanagy, J. R.: Chemistry of collagen, U. S. Department of Commerce, Circular of National Bureau of Standards C458, May, 1947.
- 1029. Kane, L. W., and Foley, G. E.: Streptomycin therapy in 52 cases of bacterial infection, New England J. Med. 237: 531, 1947.
- 1030. Kaplan, A.: Neurofibroma of cauda equina causing recurrent "sciatica" for 20 years, Bull. Hosp. Joint Dis. 8: 155 (Oct.) 1947.
- 1031. Kaplan, A.: Herniated intervertebral discs producing contralateral symptoms and signs; report of 2 cases, Bull. Hosp. Joint Dis. 10: 207 (Oct.) 1949.
- 1032. Kaplan, E., Joseph, N. R., Reed, C. I., and Sheffler, P.: Effects of inhibitor combinations on membrane potentials of synovialis, Am. J. Physiol. 159: 505 (Dec.) 1949.
- 1033. Kaplan, E. B.: Posterior neurectomies for relief of painful hip joints, Bull. Hosp. Joint Dis. 9: 48 (Apr.) 1948.
- 1034. Kaplan, E. B.: Obturator nerve avulsion in treatment of painful hip joints, S. Clin. North America 28: 473 (Apr.) 1948.
- 1035. Kaplan, E. B.: Resection of the obturator nerve for relief of pain in arthritis of the hip joint, J. Bone and Joint Surg. 30A: 213 (Jan.) 1948.
- 1036. Kaplan, E. B.: Embryological development of tendinous apparatus of fingers; relation to function, J. Bone and Joint Surg. 32A: 820 (Oct.) 1950.
- 1936a. Karelitz, S.: Serum sickness, Ann. New York Acad. Sc. 50: 705 (Dec.) 1949.
- 1037. Karlson, J. L., and Barker, H. A.: Biosynthesis of uric acid labeled with radioactive carbon, J. Biol. Chem. 177: 597 (Feb.) 1949.

1038. Karpovich, P. V., Starr, M. P., Kimbro, R. W., Stoll, C. G., and Weiss, R. A.: Physical reconditioning after rheumatic fever, J. A. M. A. 130: 1198 (Apr.) 1946.

1039. Kasich, A. M.: Clinical and roentgenologic aspects of esophageal lesions in scleroderma; report of 6 cases, Am. J. Digest. Dis. 16: 405 (Nov.) 1949.

1040. Kass, E. H., and Finland, M.: The effect of ACTH on induced fever, New England J. Med. 243: 693 (Nov.) 1950.

1041. Katz, K. H., and Berk, M. S.: Episacroiliac lipoma as a cause of low-back pain, New England J. Med. 243: 851 (Nov.) 1950.

1042. Kaufman, P., Beck, R. D., and Wiseman, R. D.: Vitamin D ("ertron") therapy in arthritis; treatment followed by massive, metastatic calcification, renal damage and death, J. A. M. A. 134: 688 (June) 1947; correction 134: 971 (July) 1947.

1043. Kavanaugh, D. E.: Non-surgical orthopedic management of rheumatoid arthritis, J. M. Soc. New Jersey 46: 421 (Sept.) 1949.

1044. Keith, J. D.: Diagnosis of rheumatic fever and rheumatic heart disease, Canad. J. Pub. Health 38: 390 (Aug.); 428 (Sept.) 1947.

1045. Keith, J. D., and Pequegnat, L. A.: Some observations on prevalence of rheumatic heart disease in Canada, Canad. J. Pub. Health 38: 111 (Mar.) 1947.

1046. Kelikian, H., and Lewis, E. K.: Arthrograms, Radiology 52: 465 (Apr.) 1949.

1047. Kelley, V. C., Good, R. A., and McQuarrie, I.: Serum mucoproteins in children in health and disease with special reference to rheumatic fever, Pediatrics 5: 824 (May) 1950.

1048. Kellgren, J. H.: Deep pain sensibility, Lancet 1: 943 (June) 1949.

1049. Kellgren, J. H., and Ball, J.: Tendon lesions in rheumatoid arthritis; clinico-pathologic study, Ann. Rheumat. Dis. 9: 48 (Mar.) 1950.

1050. Kellgren, J. H., and McGowan, A. J.: On behavior of deep and cutaneous sensibility during nerve blocks, Clin. Sc. 7: 1 (July) 1948.

1051. Kellgren, J. H., McGowan, A. J., and Hughes, E. S. R.: On deep hyperalgesia and cold pain, Clin. Sc. 7: 13 (July) 1948.

1052. Kellgren, J. H., and Samuel, E. P.: Sensitivity and innervation of articular capsule, J. Bone and Joint Surg. 32B: 84 (Feb.) 1950.

1053. Kelly, M.: Nature of fibrositis; study of causation of myalgic lesion (rheumatic, traumatic, infective), Ann. Rheumat. Dis. 5: 69 (Mar.) 1946.

1054. Kelly, M.: Nature of fibrositis; multiple lesions and neural hypothesis, Ann. Rheumat. Dis. 5: 161 (Sept.) 1946.

1055. Kelly, M.: Fibrositis and common pains of daily practice, M. J. Australia 2: 480 (Oct.) 1946.

1056. Kelly, M.: New treatment of rheumatoid arthritis, M. J. Australia 1: 219 (Feb.) 1948.

1057. Kelly, M.: Interstitial neuritis and the neural theory of fibrositis, Ann. Rheumat. Dis. 7: 89 (June) 1948.

1058. Kelly, M.: The prevention of deformity in rheumatic disease, M. J. Australia 2: 1 (July) 1950.

1059. Kemp, F. H., and Wilson, D. C.: Further report on factors in etiology of osteochondritis of spine, Brit. J. Radiol. 21: 449 (Sept.) 1948.

1060. Kemp, F. H., and Wilson, D. C.: Some factors in the actiology of osteochondritis of the spine; a report on two families, Brit. J. Radiol. 20: 410 (Oct.) 1947.

1061. Kendall, D.: Aetiology, diagnosis, and treatment of prolapsed intervertebral disk, with review of 300 cases of sciatica, Quart. J. Med. 16: 157 (July) 1947.

1062. Kendall, E. C.: Some observations on the hormone of the adrenal cortex designated compound E, Proc. Staff Meet., Mayo Clin. 24: 298 (May) 1949.

1063. Kendell, H. W., Polley, H. F., and Krusen, F. H.: Physical medicine in the home treatment of arthritis, Rheumatism 3: 86 (April-May-June) 1947.

1064. Kenin, A.: Tuberculosis of the subdeltoid bursa, Bull. Hosp. Joint Dis. 7: 28 (Apr.) 1946.

- 1065. Kerr, W. J., and Cavelti, P. A.: New immunologic aspects of pathogenesis of glomerulonephritis and rheumatic fever, Tr. A. Am. Physicians 60: 264, 1947.
- 1067. Kersley, G. D.: Diagnosis and treatment of rheumatoid arthritis, Bristol Med.-Chir. J. 63: 11, 1946.
- 1068. Kersley, G. D.: Acute arthritis in adults, Brit. J. Phys. Med. 9: 98 (July-Aug.) 1946.
- 1069. Kersley, G. D.: Modern view of gold treatment in rheumatoid arthritis, M. Press 216: 296 (Oct.) 1946.
- 1070. Kersley, G. D.: Pain and its problems; pain in rheumatic diseases, Practitioner 159: 60 (July) 1947.
- 1071. Kersley, G. D.: The present status of gold therapy in rheumatoid arthritis, Practitioner 161: 158 (Sept.) 1948.
- 1072. Kersley, G. D.: Symposium on rheumatic disorders; rheumatoid disease, Clin. J. 79: 85 (Apr.) 1950.
- 1073. Kersley, G. D., and Mandel, L.: Steroid therapy in rheumatoid arthritis; a further report, Lancet 1: 1153 (June) 1950.
- 1074. Kersley, G. D., Mandel, L., and Jeffrey, M. R.: Steroid therapy in rheumatoid arthritis, Lancet 1: 703 (Apr.) 1950.
- 1075. Kersley, G. D., Mandel, L., and Jeffrey, M. R.: Gout: an unusual case with softening and subluxation of the first cervical vertebra and splenomegaly. Result of ACTH administration and eventual post-mortem findings, Ann. Rheumat. Dis. 9: 282 (Dec.) 1950.
- 1076. Kersley, G. D., Mandel, L., Jeffrey, M. R., Desmarais, M. H. L., and Bene, E.: Insulin and E. C. T. in treatment of rheumatoid arthritis; report on a pilot series of cases, Brit. M. J. 11: 855, 1950.
- 1077. Kersley, G. D., and Simpson, N. R. W.: Clinical trial of calcium ortho-iodoxy benzoate, Ann. Rheumat. Dis. 9: 174 (June) 1950.
- 1078. Kessler, H.: Physical medicine in the treatment of arthritis, New York State J. Med. 47: 1244 (June) 1947.
- 1079. Kesson, C. M., Morris, N., and McCutcheon, A.: Generalized osteoporosis in old age, Ann. Rheumat. Dis. 6: 146 (Sept.) 1947.
- 1080. Kestler, O. C.: New method of local treatment of rheumatoid and traumatic affections of joints, with emphasis on a new approach in the management of arthritis and allied conditions, Geriatrics 1: 159 (Mar.-Apr.) 1946.
- 1081. Kestler, O. C.: Early epiphysial growth arrest about the knee joint following various infectious lesions of hip, Bull. Hosp. Joint Dis. 8: 94 (Apr.) 1947.
- 1082. Key, J. A.: Treatment of chronic arthritis, Proc. California Acad. Med. 8: 31, 1941-44.
- 1083. Key, J. A.: Idiopathic low back pain and sciatica; 25 years ago and now, Bull. Johns Hopkins Hosp. 80: 217 (May) 1947.
- 1084. Key, J. A.: Calcium deposits in the vicinity of the shoulder and of other joints, Ann. Surg. 129: 737 (June) 1949.
- 1085. Key, J. A.: Intervertebral-disc lesions in children and adolescents, J. Bone and Joint Surg. 32A: 97 (Jan.) 1950.
- 1086. Key, J. A.: The diagnosis and treatment of intervertebral disc lesions in the low back, J. Oklahoma M. A. 43: 198 (May) 1950,
- 1087. Key, J. A.: Diseases of bones and joints; orthopedic surgery, Ann. Rev. Med. 1: 257, 1950.
- 1088. Key, J. A.: Surgical revision of arthritic feet, Am. J. Surg. 79: 667 (May) 1950.
- 1089. Key, J. A., and Ford, L. T.: Experimental intervertebral disc lesions, J. Bone and Joint Surg. 30A: 621 (July) 1948.
- 1090. Key, J. A., and Reynolds, F. C.: Intrapelvic obturator neurectomy for the relief of chronic arthritis of the hip, Surgery 24: 959 (Dec.) 1948.
- 1091. Key, L. A.: Diagnosis and modern treatment of tuberculosis of the hip joint, M. Press 216: 416 (Dec.) 1946.

1092. Khoury, E. N.: Reiter's syndrome; report of 2 cases with response in one to large doses of mapharsen, J. Urol. 58: 268 (Oct.) 1947.

1093. Kidner, F. C.: Low back pain and sciatica from a conservative standpoint, S. Clin. North America 28: 1233 (Oct.) 1948.

1094. Kilham, L.: Infection caused by Streptobacillus moniliformis; report of 2 cases following rat bites, New England J. Med. 236: 969 (June) 1947.

1095. King, B. G.: Clinical diagnosis of periarteritis nodosa; a report of 4 cases, Ann. Int. Med. 32: 466 (Mar.) 1950.

1096. King, F. H.: Protracted course in periarteritis nodosa, J. Mt. Sinai Hosp. 15: 97 (July-Aug.) 1948.

1097. King, R. A.: Vitamin E therapy in Dupuytren's contracture; examination of claim that vitamin therapy is successful, J. Bone and Joint Surg. 31B: 443 (Aug.) 1949.

1098. King-Lewis, F. L.: Two cases of Ehler-Danlos syndrome, Proc. Roy. Soc. Med. 39: 135 (Jan.) 1946.

1099. Kinsella, R. A.: Differential diagnosis and treatment of arthritis, Postgrad. Med. 4: 322 (Oct.) 1948.

1100. Kipkie, G. F.: Possible role of infection in production of periarteritis nodosa in hypertensive rabbits, Arch. Path. 50: 98 (July) 1950.

1101. Kirgis, H. D., and Reed, A. F.: Significant anatomic relations in the syndrome of the scalene muscles, Ann. Surg. 127: 1182 (June) 1948.

1102. Kirk, T. R.: Phenylethylhydantoin in the treatment of Sydenham's chorea, New York State J. Med. 48: 2165 (Oct.) 1948.

1103. Kirkpatrick, J. E.: Injury vs. gout, Indust. Med. 18: 464 (Nov.) 1949.

1104. Kirschner, L., and Gallagher, D. J. A.: Studies on the pathogenesis of rheumatic fever. The antistreptolysin titre in acute tonsillitis, in patients admitted for tonsillectomy, in rheumatic fever and in control groups, New Zealand M. J. 49: 118 (Apr.) 1950.

1105. Kirschner, L., and Martin, K.: Studies on the pathogenesis of rheumatic fever, II, New Zealand M. J. 49: 713 (Dec.) 1950.

1106. Kisch, E.: Treatment of tuberculous arthritis, Am. Rev. Tuberc. 53: 533 (June) 1946.

1107. Kissane, R. W., Fidler, R. S., and Clark, T. E.: Liver dysfunction in rheumatic heart disease; preliminary report, Am. J. M. Sc. 213: 410 (Apr.) 1947.

1108. Klein, I.: Treatment of peritendinitis calcarea of shoulder joint by roentgen irradiation; report of 100 cases, Am. J. Roentgenol. 56: 366 (Sept.) 1946.

1109. Kleinberg, S.: Calcareous bursitis, New York State J. Med. 49: 171 (Jan.) 1949.

1110. Kleinberg, S.: Bilateral osteochondritis dissecans of the patella, J. Bone and Joint Surg. 31A: 185 (Jan.) 1949.

1111. Klemperer, P.: Diseases of the collagen system, Bull. New York Acad. Med. 23: 581, 1947.

1112. Klemperer, P.: Pathogenesis of lupus erythematosus and allied conditions, Ann. Int. Med. 28: 1 (Jan.) 1948.

1113. Klemperer, P.: The concept of collagen diseases, Am. J. Path. 26: 505 (July) 1950.

1114. Klemperer, P., Gueft, B., and Lee, S.: Nucleic acid depolymerization in systemic lupus erythematosus, J. Mt. Sinai Hosp. 16: 61 (May-June) 1949.

1115. Klemperer, P., Gueft, B., Lee, S. L., Leuchtenberger, C., and Pollister, A. W.: Cytochemical changes of acute lupus erythematosus, Arch. Path. 49: 503 (May) 1950.

1116. Kline, C. L., and Highsmith, L. S.: Toxic psychosis resulting from penicillin, Ann. Int. Med. 28: 1057 (May) 1948.

1117. Kline, E. M.: Hypertrophic osteoarthropathy; case report, Am. J. Roentgenol. 54: 519 (Nov.) 1945.

1118. Klinefelter, E. W.: Ossifications associated with a chronic strain of the tibial collateral ligament from roller-skating, J. Bone and Joint Surg. 29: 237 (Jan.) 1947.

 Kling, D. H.: Desoxycorticosterone acetate and ascorbic acid injections in rheumatoid arthritis, J. A. M. A. 143: 791 (July) 1950.

- 1120. Kling, D. H.: Failure of antireticular cytotoxic serum in arthritis, J. Lab. and Clin. Med. 33: 1289 (Oct.) 1948.
- 1121. Kling, D. H., Vento, J. P., and Sashin, D.: Gold therapy in rheumatoid arthritis in the United States, Rheumatism 5: 56 (Oct.) 1949.
- 1122. Knowelden, J.: Mortality from rheumatic heart disease in children and young adults in England and Wales, Brit. J. Social Med. 3: 29 (Jan.) 1949.
- 1123. Kobak, M. W., and Perlow, S.: Xanthomatous giant cell tumors arising in soft tissue; report of instance of malignant growth, Arch. Surg. 59: 909 (Oct.) 1949.
- 1124. Koenig, L. J., Weaver, T. S., Childers, A., and Woods, H. S.: Rheumatic fever in Tennessee, South. M. J. 43: 199 (Mar.) 1950.
- 1125. Kohn, K. H., Milzer, A., and MacLean, H.: Oral penicillin prophylaxis of recurrences; interim report on method after a 3 year study, J. A. M. A. 142: 20 (Jan.) 1950.
- 1126. Korb, H., and Brown, E. A.: Reiter's disease; case successfully treated with aureomycin, Arch. Dermat. and Syph. 62: 391 (Sept.) 1950.
- 1127. Korvin, H. G.: Early clinical diagnosis of common hip-diseases in children, M. Press 217: 502 (June) 1947.
- 1128. Koteen, H.: Lymphogranuloma venereum, Medicine 24: 1, 1945.
- 1129. Kottke, F. J.: Physical treatment of backache, J. A. M. A. 139: 1055 (Apr.) 1949.
- 1130. Kovacs, R.: Physical therapy in chronic arthritis, M. Clin. North America 30: 623 (May) 1946.
- 1131. Krauel, L. H.: Penicillin reaction; report of case, U. S. Nav. M. Bull. 46: 749 (May) 1946.
- 1132. Kridelbaugh, W. W., and Wyman, A. C.: Osgood-Schlatter's disease, Am. J. Surg. 75: 553 (Apr.) 1948.
- 1133. Kristoff, F. V., and Odom, G. L.: Ruptured intervertebral disk in cervical region; report of 20 cases, Arch. Surg. 54: 287 (Mar.) 1947.
- 1134. Krogh, H. W.: Dental manifestation of scleroderma; report of case, J. Oral Surg. 8: 242 (July) 1950.
- 1135. Krueger, F. J.: Osteoma complicated by myositis ossificans; a case report, Mil. Surgeon 107: 44 (July) 1950.
- 1136. Krumwiede, E.: Penicillin resistance of nonhemolytic streptococci from rheumatic children receiving prophylactic penicillin, Pediatrics 4: 634 (Nov.) 1949.
- 1137. Krusen, F. H.: Physical medicine and rehabilitation; organization of physical medicine program and its development in relation to occupational therapy, Occup. Therapy 25: 111 (Aug.) 1946.
- 1138. Kugelmass, I. N.: Vitamin P in rheumatic epistaxis, Arch. Otolaryng. 46: 684 (Nov.) 1947.
- 1139. Kuhn, H. H., and Neill, R. G.: Results of removal of ruptured intervertebral discs and combined disc-fusion operations; analysis of 288 operations, South. M. J. 39: 745 (Sept.) 1946.
- 1140. Kuhns, J. G.: Medical progress: surgery in chronic arthritis, New England J. Med. 240: 605 (Apr.) 1949.
- 1141. Kuhns, J. G., and Potter, T. A.: Nylon arthroplasty of the knee joint in chronic arthritis, Surg., Gynec. and Obst. 91: 351 (Sept.) 1950.
- 1142. Kuhns, J. G., and Morrison, S. L.: Twelve years' experience in roentgenotherapy for chronic arthritis, New England J. Med. 235: 399 (Sept.) 1946.
- 1143. Kulowski, J.: Gaucher's disease in bone, Am. J. Roentgenol. 63: 840 (June) 1950.
- 1144. Kulwin, M. H., Feldman, W. H., Hinshaw, H. C., and Montgomery, H.: Sarcoidosis; a clinical and laboratory study of 17 cases, Minnesota Med. 32: 989 (Oct.) 1949.
- 1145. Kurtz, C. M.: Prolonged rest vs. ambulatory treatment of rheumatic fever, Wisconsin M. J. 48: 498 (June) 1949.
- 1146. Kurz, E. R. H., and Loud, M. W.: Coccidioidomycosis in New England, New England J. Med. 237: 610 (Oct.) 1947.

- 1147. Kuttner, A. G., and Markowitz, M.: The diagnosis of mitral insufficiency in rheumatic children, Am. Heart J. 35: 718 (May) 1948.
- 1148. Kuzell, W. C.: Ankylosing spondylarthritis (Marie-Strümpell-Bechterew disease), Stanford M. Bull. 6: 324 (May) 1948.
- 1149. Kuzell, W. C.: Complications of gold therapy and their management, California Med. 71: 2 (Aug.) 1949.
- 1150. Kuzell, W. C., and Davison, R. A.: Serum lysolecithin in rheumatoid arthritis, pregnancy and jaundice and in normal persons, J. Lab. and Clin. Med. 31: 1223 (Nov.) 1946.
- 1151. Kuzell, W. C., and Dreisbach, R. H.: Tests of possible antagonism of gold for histamine toxicity and certain allergic reactions, Proc. Soc. Exper. Biol. and Med. 67: 157, 1948.
- 1152. Kuzell, W. C., and Gardner, G. M.: ACTH, pregnenolone, glutathione and gonadotropins in experimental polyarthritis, Stanford M. Bull. 8: 83 (May) 1950.
- 1153. Kuzell, W. C., and Gardner, G. M.: Salicylazosulfapyridine (Salazopyrin or Azopyrin) in rheumatoid arthritis and experimental polyarthritis, California Med. 73: 476 (Dec.) 1950.
- 1154. Kuzell, C., Gardner, G. M., and Fairley, DeL. M.: Aureomycin in experimental polyarthritis with preliminary trials in clinical arthritis, Proc. Soc. Exper. Biol. and Med. 71: 631 (Aug.) 1949.
- 1155. Kuzell, W. C., and Mankle, E. A.: Cortisone acetate and terramycin in polyarthritis of rats, Proc. Soc. Exper. Biol. and Med. 74: 677 (Aug.) 1950.
- 1156. Kuzell, W. C., Pillsbury, P. L., and Gellert, S. A.: The effects of 2, 3-dimercaptopropanol (BAL) on toxicity and excretion of gold, Stanford M. Bull. 5: 197 (Nov.) 1947.
- 1157. Kuzell, W. C., and Schaffarzick, R. W.: Cortisone acetate in 32 cases: preliminary clinical observations, Stanford M. Bull. 8: 125 (Aug.) 1950.
- 1158. Kuzell, W. C., and Schaffarzick, R. W.: Oral administration of cortisone acetate, Stanford M. Bull. 8: 212 (Nov.) 1950.
- 1159. Kyle, L. H., and Crain, D. C.: The clinical and metabolic effects of progesterone and anhydrohydroxy-progesterone in rheumatoid arthritis, Ann. Int. Med. 32: 878 (May) 1950.
- 1160. Kyser, F. A., McCarter, J. C., and Stengle, J.: Effect of antihistamine drugs upon serum-induced myocarditis in rabbits, J. Lab. and Clin. Med. 32: 379 (Apr.) 1947.
- 1161. Labensky, A.: Penicillin in rat-bite fever; a case report, Connecticut M. J. 10: 557 (July) 1946.
- 1162. Lahz, J. R. S.: Concerning the pathology and treatment of tennis elbow, M. J. Australia 2: 737 (Dec.) 1947.
- 1163. Laipply, T. C., and O'Neill, J. B.: Vascular lesions in rheumatic fever, Quart. Bull., Northwestern Univ. M. School 21: 211, 1947.
- 1164. Lamb, J. H., Lain, E. S., Keaty, C., and Hellbaum, A.: Steroid hormones; metabolic studies in dermatomyositis, lupus erythematosus and polymorphic light-sensitive eruptions, Arch. Dermat. and Syph. 57: 785 (May) 1948.
- 1165. Landmann, H. R., and Kersten, J. R.: Arthropathic psoriasis, Am. Pract. and Digest Treat. 1: 509 (May) 1950.
- 1166. Langley, F. A.: Nature of Still's disease, with report of case, Arch. Dis. Childhood 20: 155 (Dec.) 1945.
- 1167. Langston, H. H.: Brittain method of arthrodesis of hip, Proc. Roy. Soc. Med. 40: 895 (Dec.) 1947.
- 1168. Lanier, R. R.: Effects of exercise on knee-joints of inbred mice, Anat. Rec. 94: 311 (Mar.) 1946.
- 1169. Lansbury, J.: Recognition and management of gout, M. Clin. North America 30: 597 (May) 1946.
- 1170. Lansbury, J.: Infection and rheumatoid arthritis, M. Clin. North America 34: 1693 (Nov.) 1950.

- 1171. Lansbury, J., Crosby, W. R., and Bello, C. T.: Precipitin reaction of serum from cases of rheumatoid arthritis with homologous connective tissue extracts, Am. J. M. Sc. 220: 414 (Oct.) 1950.
- 1172. Lapidus, P. W., and Seidenstein, H.: Chronic nonspecific tenosynovitis with effusion about ankle; report of 3 cases, J. Bone and Joint Surg. 32A: 175 (Jan.) 1950.
- 1173. Lapin, L., and Starkey, H.: Hyaluronidase inhibitory substances in sera from patients with rheumatic disease, Canad. M. A. J. 60: 468 (May) 1949.
- 1174. Laqueur, G. L.: Cytological changes in human hypophyses after cortisone and ACTH treatment, Science 112: 429 (Oct.) 1950.
- 1175. Larsen, N. P.: Arthritis and rainfall, Plantation Health (no. 2) 10: 25 (Apr.) 1946.
- 1176. Lasserre, C., Pauzat, D., and Derennes, R.: Osteoarthritis of trapezio-metacarpal joint, J. Bone and Joint Surg. 31B: 534 (Nov.) 1949.
- 1177. Lattomus, W. W., and Hunter, L. M.: Roentgen therapy of subdeltoid bursitis; review of 235 cases, Delaware State M. J. 21: 115 (July) 1949.
- 1178. Laur, W. E.: Articular manifestations of lymphogranuloma venereum, Urol. and Cutan. Rev. 53: 543 (Sept.) 1949.
- 1179. Lavner, G.: Osteochondritis dissecans; analysis of 42 cases and review of literature, Am. J. Roentgenol. 57: 56 (Jan.) 1947.
- 1180. Law, S. G.: Interview therapy of psychosomatic arthritis, Rheumatism 5: 38 (Apr.) 1949.
- 1181. Law, W. A.: Hip joint reconstruction by vitallium mould arthroplasty, Rheumatism 3: 157 (Jan.) 1948.
- 1182. Law, W. A.: Post-operative study of vitallium mould arthroplasty of hip joint, J. Bone and Joint Surg. 30B: 76 (Feb.) 1948.
- 1183. Law, W. A.: The surgical treatment of rheumatoid arthritis, Practitioner 161: 163 (Sept.) 1948.
- 1184. Law, W. A.: Surgery in treatment of ankylosing spondylitis, Proc. Roy. Soc. Med. 41: 251 (Apr.) 1948.
- 1185. Law, W. A.: Surgical procedures in treatment of chronic arthritis of spine, Ann. Roy. Coll. Surgeons, England 6: 56 (Jan.) 1950.
- 1186. Lawrence, J. S.: Plasma viscosity, Ann. Rheumat. Dis. 8: 209 (Sept.) 1949.
- 1187. Lees, R.: Treatment of sulphonamide-resistant gonorrhoea by penicillin, Brit. M. J. 1: 605 (Apr.) 1946.
- 1188. Lefevre, W. I.: Painful shoulder—its diagnosis and treatment, Mississippi Valley M. J. 70: 230 (Nov.) 1948.
- 1189. Leibholz, E.: A medical treatment for acute calcifying bursitis (bursoarthritis), New York State J. Med. 50: 565 (Mar.) 1950.
- 1190. Lennon, W., and Chalmers, I. S.: Ankylosing spondylitis, Lancet 1: 12 (Jan.) 1948.
- 1191. Lenzer, A. R., Lockie, L. M., and Becker, C. F.: Acute yellow atrophy following cinchophen administration; report of case, New England J. Med. 236: 500 (Apr.) 1947.
- 1192. Leonard, M. H.: Injuries of the lateral ligaments of the ankle; a clinical and experimental study, J. Bone and Joint Surg. 31A: 373 (Apr.) 1949.
- 1193. Leopold, H. N.: ACTH and colchicine in therapy of gout; report of a case of acute gouty arthritis, Texas J. Med. 46: 710 (Sept.) 1950.
- 1194. Lepow, H., Rubenstein, L., Woll, F., and Greisman, H.: A spontaneously precipitable protein in human sera, with particular reference to the diagnosis of polyarteritis nodosa, Am. J. Med. 7: 310 (Sept.) 1949.
- 1195. Lerner, H. H., and Gazin, A. I.: Interarticular isthmus hiatus (spondylolysis), Radiology 46: 573 (June) 1946.
- 1196. Lerner, H. H., Watkins, M. B., and Resnick, B.: Osteochondritis dissecans of supratrochlear septum of humerus, Am. J. Roentgenol. 55: 717 (June) 1946.
- 1197. LeVay, D.: Place of orthopaedic surgery in treatment of chronic rheumatic conditions of hip and knee joints, Rheumatism 6: 99 (July) 1950.

1198. LeVay, D., and Loxton, G. E.: Deoxycortone acetate and ascorbic acid in the treatment of rheumatoid arthritis, Lancet 2: 1134 (Dec.) 1949.

1199. LeVay, D., and Loxton, G. E.: Clinical observations with deoxycortone and ascorbic acid, Lancet 1: 209 (Feb.) 1950.

1200. Levey, J. S., and Levey, Stanley: Chemotherapy of joint involvement in mice produced by Streptobacillus moniliformis, Proc. Soc. Exper. Biol. and Med. 68: 314 (June) 1948.

1201. Levey, P.: Use of intracain in oil for the relief of pain involving the musculo-skeletal system, Rheumatism 4: 234 (Oct.) 1948.

Levi, D.: Anomalous insertion of scalenus medius muscle with forearm pain, Post-Grad.
 M. J. 24: 259 (May) 1948.

1203. Levine, B., and Civin, W. H.: Streptobacillus moniliformis bacteremia with minor clinical manifestations, Arch. Int. Med. 80: 53 (July) 1947.

1204. Levine, R., Wolfson, W. Q., and Lenel, R.: Concentration and transport of true urate in plasma of azotemic chicken, Am. J. Physiol. 151: 186 (Nov.) 1947.

1205. Levitan, B. A.: Inhibition of testicular hyaluronidase activity by rutin, Proc. Soc. Exper. Biol. and Med. 68: 566 (July-Aug.) 1948.

1206. Levy, H.: Granulocytopenic and lymphocytopenic hypersplenism associated with atrophic arthritis, Acta med. Scandinav. 129: 203, 1947.

Levy, H. B., Coffey, J. D., and Anderson, C. E., Jr.: Rheumatic pneumonitis in child-hood, Pediatrics 2: 688 (Dec.) 1948.

1208. Lewey, F. H.: The mechanism of the intervertebral disc protrusion, Surg., Gynec. and Obst. 88: 592 (May) 1949.

1209. Lewin, E., and Wassen, E.: Effect of combined injections of deoxycortone acetate and ascorbic acid on rheumatoid arthritis, Lancet 2: 993 (Nov.) 1949.

1210. Lewin, P.: The intervertebral disk syndrome, J. Internat. Coll. Surgeons 11: 137 (Mar.-Apr.) 1948.

1211. Lewin, P.: Infections of the bones and joints, Arch. Surg. 58: 189 (Feb.) 1949.

1212. Lewin, W.: Sciatica and prolapsed intervertebral disc, M. Press 214: 392 (Dec.) 1945.

1213. Lewis, R. V., and Kramer, L. I.: Serum protein, cephalin flocculation and thymol turbidity alterations in lupus erythematosus disseminatus; a case report, Rhode Island M. J. 33: 594 (Nov.) 1950.

1213a. Lewis, R. W.: Roentgen diagnosis of pigmented villonodular synovitis and synovial sarcoma of knee joint; preliminary report, Radiology 49: 26 (July) 1947.

1214. Lewy, R. B.: Dermatomyositis and scleroderma; unusual causes of dysphagia, Arch. Otolaryng. 52: 31 (July) 1950.

1215. Leys, D. G., and Swift, P. N.: Pulmonary lesions in rheumatoid arthritis, Brit. M. J. 1: 434 (Mar.) 1949.

1216. Li, C. H.: The adrenocorticotropic hormone (ACTH) of the anterior pituitary, J. Endocrinol. 6: 40 (Jan.) 1950.

1217. Libenson, L., and Wittenborn, W. F. J.: Treatment of arthritis with "anathion," J. M. Soc. New Jersey 47: 105 (Mar.) 1950.

1218. Lichtenstein, L., and Fox, L. J.: Necrotizing arterial lesions resembling those of periarteritis nodosa and focal visceral necrosis following administration of sulfathiazole; report of case, Am. J. Path. 22: 665 (July) 1946.

1219. Liebolt, F. L., Beal, J. M., and Speer, D. S.: Obturator neurectomy for painful hip, Am. J. Surg. 79: 427 (Mar.) 1950.

 Liebow, I. M., and Feil, H.: Electrocardiogram in lupus erythematosus disseminatus, Am. J. Med. 3: 44 (July) 1947.

1221. Lightbody, J. J., Price, A. E., Reveno, W. S., and VonderHeide, E. C.: Cortisone in rheumatoid arthritis; observations of 15 patients, J. Michigan M. Soc. 49: 1085 (Sept.) 1950.

- 1222. Lindblom, K., and Hultquist, G. T.: Absorption of protruded disk tissue, J. Bone and Joint Surg. 32A: 557 (July) 1950.
- 1223. Lindley, E. L., and Middleton, J. W.: Diagnosis and management of gout, Texas State J. Med. 43: 530 (Dec.) 1947.
- 1224. Lipkin, E.: Procaine in rheumatic diseases, J. Michigan M. Soc. 49: 1081 (Sept.) 1950.
- 1225. Lipman, B. L., Krasnoff, S. O., and Schless, R. A.: Acute acetylsalicylic acid intoxication, Am. J. Dis. Child. 78: 477 (Oct.) 1949.
- 1226. Lipman, M. P., and Tober, J. N.: Peripheral manifestations of visceral carcinoma, Gastroenterology 16: 188 (Sept.) 1950.
- 1227. Lisman, J. V.: Dermatomyositis with retinopathy; report of case, Arch. Ophth. 37: 155 (Feb.) 1947.
- 1228. Lloyd, W. E., and Tonkin, R. D.: Pulmonary fibrosis in generalized scleroderma, Thorax 3: 241, 1948.
- 1229. Lockie, L. M., and Norcross, B. M.: Juvenile rheumatoid arthritis, Pediatrics 2: 694 (Dec.) 1948.
- 1230. Lockie, L. M., Norcross, B. M., and George, C. W.: Treatment of 2 reactions due to gold; response of thrombopenic purpura and granulocytopenia to BAL therapy, J. A. M. A. 133: 754 (Mar.) 1947.
- 1231. Lockie, L. M., and Musgrove, E.: Physical therapy in treatment of arthritis, New York State J. Med. 47: 851 (Apr.) 1947.
- 1232. Lockwood, J. H.: Reiter's disease, Behçet's syndrome, and Stevens-Johnson disease; a study and comparison, U. S. Nav. M. Bull. 49: 41 (Jan.-Feb.) 1949.
- 1233. Logue, R. B., and Mullins, F.: Polyarteritis nodosa; report of 11 cases with review of recent literature, Ann. Int. Med. 24: 11 (Jan.) 1946.
- 1234. Lominski, I. R. W., Henderson, A. S., and McNee, J. W.: Rat-bite fever due to Strep-tobacillus moniliformis, Brit. M. J. 2: 510 (Sept.) 1948.
- 1235. Long, J. B., and Favour, C. B.: The ability of ACTH and cortisone to alter delayed type bacterial hypersensitivity, Bull. Johns Hopkins Hosp. 87: 186 (Sept.) 1950.
- 1236. Long, J. H., and Aegerter, E. E.: Lupus erythematosus and the collagen diseases, Pennsylvania M. J. 52: 1076 (July) 1949.
- 1237. LoPresti, J. M.: Juvenile rheumatoid arthritis with a report of a case in a 15 month old child, Clin. Proc. Child. Hosp. 5: 74 (Feb.) 1949.
- 1238. Love, J. G.: The disc factor in low-back pain with or without sciatica, J. Bone and Joint Surg. 29: 438 (Apr.) 1947.
- 1239. Loveland, G.: The opsonocytophagic test in brucellosis, Nebraska M. J. 33: 299 (Sept.) 1948.
- 1240. Lovell, R. R. H.; Observations on structure of clubbed fingers, Clin. Sc. 9: 299 (Aug.) 1950.
- 1241. Lovell, W. W.: Infection of the knee joint by Clostridium welchii; report of case, J. Bone and Joint Surg. 28: 398 (Apr.) 1946.
- 1242. Lovshin, L. L., and Kernohan, J. W.: Peripheral neuritis in periarteritis nodosa; clinico-pathologic study, Arch. Int. Med. 82: 321 (Oct.) 1948.
- 1243. Lowbeer, L.: Brucellosis osteomyelitis of man and animal, Proc. Staff Meet. Hillcrest Memorial Hosp., Tulsa, Oklahoma 6: 1 (Jan.) 1949.
- 1244. Lowe, G. H., Jr., and Lipscomb, P. R.: Brucellosis osteomyelitis; report of 2 cases in which shafts of long bones were involved, Surgery 22: 525 (Sept.) 1947.
- 1245. Lowenthal, J., and Gagnon, A.: Inhibition of hyaluronidase by sodium salicylate and its possible metabolites, Canad. J. Research, Sect. E 26: 200 (June) 1948.
- 1246. Lowman, E. W., and Boucek, R. J.: Reiter's disease: report of 5 cases including 2 successfully treated with hyperthermia, Ann. Int. Med. 28: 1075 (June) 1948.
- 1247. Lowry, C. F.: Comments on the observations of approximately 500 cases of rheumatic diseases in a private practice, J. Iowa M. Soc. 40: 214 (May) 1950.

1248. Loxton, G.: Recent advances in the treatment of rheumatoid arthritis, Post-Grad. M. J. 26: 447 (Aug.) 1950.

1249. Lubell, M. F.: Roentgen therapy for treatment of painful shoulder, J. Maine M. A. 41: 368 (Sept.) 1950.

 Lucchesi, M., and Lucchesi, O.: Personal experience with neostigmine therapy in rheumatoid arthritis. Ann. Rheumat. Dis. 5: 214 (Dec.) 1946.

1251. Lucchesi, M., and Lucchesi, O.: Significance of subcutaneous nodules, Ann. Rheumat. Dis. 6: 219 (Dec.) 1947.

 Lucchesi, M., and Lucchesi, O.: Rheumatoid spondylitis; a paediatric problem, Ann. Rheumat. Dis. 9: 372 (Dec.) 1950.

1253. Lucchesi, O., Lucchesi, M., and Kneese, deM. H.: The heart in rheumatoid arthritis; clinical, radiological, and electrographic study of 50 cases [Abstract] Ann. Rheumat. Dis. 7: 186 (Sept.) 1948.

1254. Lucchesi, O., Lucchesi, M., and Bailone, S.: Weltmann coagulation reaction in rheumatoid arthritis, Ann. Rheumat. Dis. 5: 78 (Mar.) 1946.

1255. Ludwig, A. O.: Emotional factors in arthritis: bearing on the care and rehabilitation of the patient, Physiotherapy Rev. 29: 339 (Aug.) 1949.

Lugiato, P. E.: Arthritis deformans; pathologic histology; research in polarized light,
 J. Bone and Joint Surg. 30A: 895 (Oct.) 1948.

1257. Lukens, F. D. W., Hollander, J. L., Brown, E. M., Jr., and DeMoor, P.: The apparent independence of the metabolic and antiarthritic effects of cortisone and ACTH, Tr. A. Am. Physicians 63: 99, 1950.

1258. Lush, B.: Some basic principles in the treatment of flexion deformity of the knee, M. Press 222: 127 (Aug.) 1949.

1259. Lush, B.: Recent advances in the treatment of the rheumatic disorders, Clin. J. 79: 102 (Apr.) 1950.

1260. Lush, B.: Some principles to be followed in the prevention of contractures, Occup Therapy 29: 215 (Aug.) 1950.

1261. Lushbaugh, C. C., Rubin, L., and Rothman, S.: Scleroderma of the intestinal tract; first report of a fatal case, Gastroenterology 11: 382 (Sept.) 1948.

1262. Lyerly, J. G., and Grizzard, V. T.: Dislocated disc of the lumbar region; statistical analysis of series of cases, South. Surgeon 14: 755 (Nov.) 1948.

1263. Lyford, J., III, Johnson, R. W., Jr., Blackman, S., and Scott, R. B.: Pathologic findings in a fatal case of disseminated granuloma inguinale with miliary bone and joint involvement, Bull. Johns Hopkins Hosp. 79: 349 (Nov.) 1946.

1264. Lyon, R. A.: The prevention of rheumatic fever, Kentucky M. J. 47: 180 (May) 1949. 1265. Lyon, R. A., Rauh, L. W., and Wolf, R. E.: Prevention of rheumatic fever in children

by use of sulfonamides, Ohio State M. J. 43: 394 (Apr.) 1947.

1266. MacConaill, M. A.: Studies in mechanics of synovial joints; fundamental principles and diadochol movements, Irish J. M. Sc., p. 190 (June) 1946.

1267. MacConaill, M. A.: Studies in mechanics of synovial joints; displacements on articular surfaces and significance of saddle joints, Irish J. M. Sc., p. 223 (July) 1946.

1268. MacConaill, M. A.: Studies in mechanics of synovial joints; hinge-joints and nature of intra-articular displacements, Irish J. M. Sc., p. 620 (Sept.) 1946.

1269. MacConaill, M. A.: Movements of bones and joints; fundamental principles with particular reference to rotation movement, J. Bone and Joint Surg. 30B: 322 (May) 1948.

1270. MacConaill, M. A.: Movements of bones and joints; synovial fluid and its assistants, J. Bone and Joint Surg. 32B: 244 (May) 1950.

1271. Macey, H. B.: Clinical review of mechanics of the low back and its relationship to low back pain, with special reference to intervertebral disc, Arizona Med. 7: 40 (Nov.) 1950.

- 1272. Mackintosh, J. M., and Knowelden, J.: Social and economic aspects of the rheumatic diseases, Brit. J. Phys. Med. 11: 177 (Nov.-Dec.) 1948.
- 1273. Macleod, J. G.: BAL in the treatment of gold toxicity, Ann. Rheumat. Dis. 7: 143 (Sept.) 1948.
- 1274. Macleod, J. G., and Phillips, L.: Hypersensitivity to colchicine, Ann. Rheumat. Dis. 6: 224 (Dec.) 1947.
- 1275. Macnab, I.: The pathogenesis of the clinical picture in sciatica, J. Roy. Army M. Corps 91: 152 (Oct.) 1948.
- 1276. MacQuiddy, E. L.: Metabolic arthritides, Nebraska M. J. 31: 192 (May) 1946.
- 1277. Madden, J. F.: Comparison of muscle biopsies and bone marrow examinations in dermatomyositis and lupus erythematosus, Arch. Dermat. and Syph. 62: 192 (Aug.) 1950.
- 1278. Madison, F. W.: Diagnostic aids in periarteritis nodosa, Am. Pract. 2: 791 (Aug.) 1948.
- 1279. Magnuson, P. B.: Technic of debridement of knee joint for arthritis, S. Clin. North America 26: 249 (Feb.) 1946.
- 1280. Magnuson, P. B., McElvenny, R. T., and Logan, C. E.: Clinical study of 180 cases of arthritis; use of steroid complex (Whittier); orthopedic and other supportive measures in chronic arthritis, J. Michigan M. Soc. 46: 71 (Jan.) 1947.
- 1281. Magoffin, R. L., Kabler, P., Spink, W. W., and Fleming, D. S.: An epidemiologic study of brucellosis in Minnesota, Pub. Health Rep. 64: 1021 (Aug.) 1949.
- 1283. Malhotra, S. L.: Gonococcal arthritis, Indian M. Gaz. 85: 187 (May) 1950.
- 1284. Maliner, M. M., and Amsterdam, S. D.: Oral penicillin in prophylaxis of recurrent rheumatic fever, J. Pediat. 31: 658 (Dec.) 1947.
- 1285. Malkin, S. A. S.: Osteoarthritic tuberculosis, Practitioner 160: 196 (Mar.) 1948.
- 1286. Manchester, R. C.: Rheumatic fever in naval enlisted personnel; effectiveness of intensive salicylate therapy in cases of acute infection, Arch. Int. Med. 78: 170 (Aug.) 1946.
- 1287. Manchester, R. C.: Rheumatic fever in naval enlisted personnel; analysis of major manifestations observed, factors involved in its occurrence and cardiac residua, Arch. Int. Med. 77: 317 (Mar.) 1946.
- 1288. Marble, H. C., Moore, A. T., and Woodhall, B.: Ruptured intervertebral discs, American Mutual Liability Insurance Co., Boston, Mass., March 1950. Industrial Medicine and Surgery.
- 1289. Marcus, M. D., and Wooldridge, W. E.: Poikilodermatomyositis (poikiloderma vasculare atrophicans); report of a case exhibiting features of panniculitis, scleroderma, periarteritis nodosa and calcinosis cutis, Arch. Dermat. and Syph. 62: 131 (July) 1950.
- 1290. Marcus, S., and Fulton, J. K.: Relation of complement to thermolabile hyaluronidase inhibitor of serum, Federation Proc. 8: 493 (Mar.) 1949.
- 1291. Margolis, H. M., Fetterman, G. H., and Caplan, P. S.: The absorption of gold from pellets of gold salts (aurothioglycolanilide) implanted subcutaneously and intramuscularly: its application in the treatment of 6 cases of rheumatoid arthritis, Am. J. M. Sc. 218: 121 (Aug.) 1949.
- 1292. Margolis, H. M., and Caplan, P. S.: The use of curare (d-tubocurarine in oil and wax) in the treatment of muscle spasm in rheumatic disorders, Ann. Int. Med. 31: 615 (Oct.) 1949.
- 1293. Margolis, H. M., and Caplan, P. S.: Treatment of acute gouty arthritis with pituitary adrenocorticotropic hormone (ACTH), J. A. M. A. 142: 256 (Jan.) 1950.
- 1294. Markowitz, H. A., and Gerry, R. G.: Temporomandibular joint disease, Oral Surg., Oral Med. and Oral Path. 2: 1309 (Oct.) 1949.
- 1295. Markowitz, M., and Kuttner, A. G.: A study of the absorption and excretion of oral penicillin in children, J. Pediat. 31: 195 (Aug.) 1947.

1296. Markson, D. E.: Prolonged treatment of rheumatoid arthritis with pituitary adrenocorticotropic hormone (ACTH), J. A. M. A. 141: 458 (Oct.) 1949.

1297. Marsden, J. A.: Tuberculosis of hip and spine; a short survey of cases, M. J. Australia 1: 696 (June) 1947.

1298. Marsden, C. M.: Analysis of 100 consecutive operations on knee and report of xanthoma of knee joint, J. Roy. Army M. Corps 89: 29 (July) 1947.

1299. Marsh, F.: Reiter's disease, Brit. M. J. 2: 275 (Aug.) 1946.

1300. Martin, A. T.: Modern concepts of rheumatic fever, Mississippi Doctor 25: 231 (Dec.) 1947; Present-day concepts of rheumatic fever, Ohio State M. J. 44: 265 (Mar.) 1948.

1301. Martin, G. M., Roth, G. M., Elkins, E. C., and Krusen, F. H.: Cutaneous temperature of extremities of normal subjects and of patients with rheumatoid arthritis, Arch. Phys. Med. 27: 665 (Nov.) 1946.

1302. Martin, J.: The diagnosis and treatment of herniation of the intervertebral disc, Chicago M. Soc. Bull. 51: 499 (Jan.) 1949.

1303. Marton, R., and Steinbrocker, O.: Congenital contracture of the fifth finger, New York State J. Med. 49: 1064 (May) 1949.

1304. Marton, R., Spitzer, N., and Steinbrocker, O.: Intravenous procaine as an analgesic and therapeutic procedure in painful, chronic neuromusculoskeletal disorders, Anesthesiology 10: 629 (Sept.) 1949.

1305. Massachusetts General Hospital case: Postrheumatic arthritis, Am. Pract. and Digest Treat. 1: 185 (Feb.) 1950.

1306. Massachusetts General Hospital case 76 and 77: Rheumatoid arthritis, Am. Pract. 3: 256 (Dec.) 1948.

1307. Massachusetts General Hospital case 88: Lupus erythematosus disseminatus, Am. Pract. 3: 439 (Mar.) 1949.

1308. Massachusetts General Hospital case 95: Vitamin D poisoning, Am. Pract. 3: 568 (May) 1949.

1309. Massachusetts General Hospital case 106: Osteo-arthropathy, Am. Pract. 4: 50 (Sept.) 1949.

1310. Massachusetts General Hospital case 33241: Periarteritis nodosa involving gall bladder and liver; infarcts of gall bladder, New England J. Med. 236: 909 (June) 1947.

1311. Massachusetts General Hospital case 33382: Periarteritis nodosa, New England J. Med. 237: 457 (Sept.) 1947.

1312. Massachusetts General Hospital case 34531: Rheumatoid arthritis, chronic, New England J. Med. 239: 1047 (Dec.) 1948.

1313. Massachusetts General Hospital case 35121: Synovioma of left knee, with metastases to vertebrae, clavicle, ribs, pelvic bones, peritoneum, abdominal lymph nodes, lungs and liver, New England J. Med. 240: 472 (Mar.) 1949.

1314. Massell, B. F.: Management of rheumatic fever and rheumatic heart disease, Minnesota Med. 31: 633 (June) 1948.

1315. Massell, B. F.: Salicylates, hormones and penicillin in the treatment of rheumatic fever, M. Clin. North America 34: 1419 (Sept.) 1950.

1316. Massell, B. F., Coen, W. B., and Jones, T. D.: Observations regarding artificially induced subcutaneous nodules in rheumatic fever patients, Pediatrics 5: 909 (June) 1950.

1317. Massell, B. F., Dow, J. W., and Jones, T. D.: Orally administered penicillin in patients with rheumatic fever, J. A. M. A. 138: 1030 (Dec.) 1948.

1318. Massell, B. F., and Warren, J. E.: Effect of pituitary adrenocorticotropic hormone (ACTH) on rheumatic fever and rheumatic carditis, J. A. M. A. 144: 1335 (Dec.) 1950.

1319. Massell, B. F., Warren, J. E., Patterson, P. R., and Lehmus, H. J.: Antirheumatic ac-

tivity of ascorbic acid in large doses; preliminary observations on 7 patients with rheumatic fever, New England J. Med. 242; 614 (Apr.) 1950.

1320. Massell, B. F., Warren, J. E., Sturgis, G. P., Hall, B., and Craige, E.: The clinical response of rheumatic fever and acute carditis to ACTH, New England J. Med. 242: 641 (Apr. and May) 1950.

1321. Mathisen, A. K., and Palmer, J. D.: Diffuse scleroderma with involvement of heart; report of case, Am. Heart J. 33: 366 (Mar.) 1947.

1322. Matis, J. D.: Reiter's disease—report of case successfully treated, New York State J. Med. 47: 1274 (June) 1947.

1323. Mauer, E. F.: On etiology of clubbing of fingers, Science 104: 555 (Dec.) 1946.

1324. Mauer, E. F.: On the etiology of clubbing of the fingers, Am. Heart J. 34: 852 (Dec.) 1947.

1325. Maunsell, K., Wrigley, F., Highton, T. C., and Holt, L. B.: The synovial membrane; some observations in normal and arthritic human joints, Ann. Rheumat. Dis. 9: 363 (Dec.) 1950.

1326. Mawson, R.: Treatment of osteoarthritis by lactic acid injection; series of 26 consecutive cases in general practice, Brit. M. J. 2: 691 (Nov.) 1946.

1327. Mayfield, F. H.: Causalgia, Am. J. Surg. 74: 522 (Nov.) 1947.

1328. McBurney, H. S.: The orthopedic treatment of tuberculosis of the spine in a military tuberculosis center, Mil. Surgeon 106: 358 (May) 1950.

1329. McCarroll, H. R., and Heath, R. D.: Tuberculosis of the hip in children; certain roent-genographic manifestations, secondary changes in the extremity, and some suggestions for program of therapy, J. Bone and Joint Surg. 29: 889 (Oct.) 1947.

1330. McCarty, A. C.: Therapeutic considerations of rheumatic diseases, Kentucky M. J. 45: 246 (July) 1947.

 McClanahan, H. H., Jr.: Medical treatment of calcification of supraspinatus tendon, Mississippi Doctor 24: 239 (Feb.) 1947.

1332. McClellan, W. S.: Physical medicine in the treatment of the aged, J. A. M. A. 137: 130 (May) 1948.

1333. McClure, D. M.: A case of generalized scleroderma simulating oesophageal carcinoma, Glasgow M. J. 31: 339 (Oct.) 1950.

1334. McComas, E.: Perthes' disease and its occurrence as familial condition, M. J. Australia 2: 584 (Oct.) 1946.

1335. McCombs, R. P., and MacMahon, H. E.: Dermatomyositis associated with metastasizing bronchogenic carcinoma; clinicopathological conference, M. Clin. North America 31: 1148 (Sept.) 1947.

1336. McCorkle, H. J., Silvani, H., Stern, W. E., and Warmer, H.: Clinical experiences with the use of penicillin treatment of infections involving bones and joints, Surg., Gynec. and Obst. 84: 269 (Mar.) 1947.

1337. McCormick, R. V.: Periarteritis occurring during propylthiouracil therapy, J. A. M. A. 144: 1453 (Dec.) 1950.

1338. McCort, J. J., Wood, R. H., Hamilton, J. B., and Erlich, D. E.: Sarcoidosis; clinical and roentgenologic study of 28 proved cases, Arch. Int. Med. 80: 293 (Sept.) 1947.

1339. McCracken, J. P., Owen, P. S., and Pratt, J. H.: Gout; still a forgotten disease, J. A. M. A. 131: 367 (June) 1946.

1340. McCreight, W. G., and Montgomery, H.: Cutaneous changes in lupus erythematosus; histopathologic aspects, with special reference to vascular changes, Arch. Dermat. and Syph. 61: 1, 1950.

1341. McCue, C. M., and Galvin, L. F.: Preliminary report on rheumatic fever in Virginia, J. Pediat. 33: 467 (Oct.) 1948.

1342. McCullough, N. B.: Laboratory tests in the diagnosis of brucellosis, Am. J. Pub. Health 39: 866 (July) 1949. 1343. McCurrach, A. C., Norton, G. I., and Bouchard, J.: Subacromial bursitis; classification and evaluation of results of roentgen therapy, Canad. M. A. J. 61: 39 (July) 1949.

1344. McDermott, W. V., Fry, E. G., Brobeck, J. R., and Long, C. N. H.: Release of adrenocorticotrophic hormone by direct application of epinephrine to pituitary grafts, Proc. Soc. Exper. Biol. and Med. 73: 609 (Apr.) 1950.

1345. McDermott, W. V., Fry, E. G., Brobeck, J. R., and Long, C. N. H.: Mechanism of control of adrenocorticotrophic hormone, Yale J. Biol, and Med. 23: 52 (Sept.) 1950.

1346. McEwen, C.: Development of the campaign against the rheumatic diseases, J. M. Soc. New Jersey 46: 510 (Nov.) 1949.

1347. McEwen, C.: The use of cortisone and ACTH in the treatment of rheumatic fever, Bull. Rheumat. Dis. 1: 3 (Oct.) 1950.

1348. McEwen, C., and Bunim, J. J.: Effects of cortisone and ACTH on various types of rheumatic diseases, Tr. A. Am. Physicians 63: 79, 1950.

1349. McEwen, C., Bunim, J. J., Baldwin, J. S., Kuttner, A. G., Appel, S. B., and Kaltman, A. J.: The effect of cortisone and ACTH on rheumatic fever, Bull. New York Acad. Med. 62: 212 (Apr.) 1950.

1350. McEwen, C., Bunim, J. J., Sokoloff, L., Bien, E. J., Wilens, S. L., and Ziff, M.: Histological and chemical changes in skeletal muscle of patients with rheumatic and non-rheumatic diseases, Tr. A. Am. Physicians 62: 279, 1949.

1351. McGowan, J. M., and Velinsky, M.: Costoclavicular compression; relation to the scalenus anticus and cervical rib syndromes, Arch. Surg. 59: 62 (July) 1949.

1352. McInnes, J. D.: Periarthritis of shoulder, Canad. M. A. J. 55: 131 (Aug.) 1946.

1353. McIntosh, H. C.: Roentgen therapy in shoulder pain; a report of 50 cases, J. Am. M. Women's A. 3: 277 (July) 1948.

1354. McKeown, E. F.: Experimental serum carditis and its relationship to rheumatic fever, J. Path. and Bact. 59: 547 (Oct.) 1947.

1355. McKeown, E. F.: The pathology of rheumatic fever, Ulster M. J. 14: 97 (Nov.) 1945.
1356. McLaughlin, H. L.: Lesions of musculotendinous cuff of shoulder; observations on pathology, course and treatment of calcific deposits, Ann. Surg. 124: 354 (Aug.)

1357. McLaughlin, H. L.: Common shoulder injuries; diagnosis and treatment, Am. J. Surg. 74: 282 (Sept.) 1947.

1358. McMillan, J. C., Jr.: Seventy-eight hundred scarlet fever patients, U. S. Nav. M. Bull. 46: 89 (Jan.) 1946.

1359. McMillan, R. L., and Jones, C. C.: Rheumatic heart disease in northwest North Carolina, North Carolina M. J. 11: 105 (Mar.) 1950.

1361. Mead, N. C.: Calcifying tendinitis of the shoulder, Quart. Bull., Northwestern Univ. M. School 22: 270, 1948.

1362. Means, M. G., and Brown, N. W.: Secondary hypertrophic osteoarthropathy in congenital heart disease, Am. Heart J. 34: 262 (Aug.) 1947.

1363. Medvei, V. C.: Extensive interstitial calcinosis with osteoporosis and sclerodermadermatomyositis, Lancet 2: 708 (Dec.) 1945.

1364. Meherin, J. M., and Cooper, C. E.: Tennis elbow, Am. J. Surg. 80: 622 (Nov.) 1950.

1365. Mehl, J. W., Humphrey, J., and Winzler, R. J.: Mucoproteins of human plasma; electrophoretic studies of mucoproteins from perchloric acid filtrates of plasma, Proc. Soc. Exper. Biol. and Med. 72: 106 (Oct.) 1949.

1366. Mendell, T. H., and Prose, P. H.: Severe allergic reactions to penicillin, Am. J. M. Sc. 212: 541 (Nov.) 1946.

1367. Mennell, J.: Manipulation of stiff joints, Arch. Phys. Med. 28: 685 (Nov.) 1947.

1368. Mercer, W.: Tennis elbow, Practitioner 164: 293 (Apr.) 1950.

1369. Meredith, J. M.: Familial sciatica due to herniated discs, South. Surgeon 14: 258 (Apr.) 1948.

1370. Meschan, I., and McGaw, W. H.: Newer methods of pneumoarthrography of the knee

- with an evaluation of the procedure in 315 operated cases, Radiology 49: 675 (Dec.) 1947.
- 1371. Mettier, S. R.: Classification and treatment of rheumatic diseases with special emphasis on infectious and rheumatoid arthritis, Am. J. Orthodontics (Oral Surg. Sect., no. 8) 32: 440 (Aug.) 1946.
- 1372. Mettier, S. R.: Classification of the rheumatic diseases with special emphasis on the diagnosis and treatment of rheumatoid arthritis, Am. Pract. 4: 196 (Dec.) 1949.
- 1373. Mettier, S. R., McBride, A., and Li, J.: Thrombocytopenic purpura complicating gold therapy for rheumatoid arthritis; Report of three cases with spontaneous recovery and one case with recovery following splenectomy, Blood 3: 1105 (Oct.) 1948.
- 1374. Meyer, K.: The biological significance of hyaluronic acid and hyaluronidase, Physiol. Rev. 27: 335 (July) 1947.
- 1375. Meyer, K.: Highly viscous sodium hyaluronate, J. Biol. Chem. 176: 993 (Nov.) 1948.
- 1376. Meyer, K.: The mucopolysaccharides of the interfibrillar substance of the mesenchyme, Ann. New York Acad. Sc. 52: 961 (May) 1950.
- 1377. Meyer, K., and Ragan, C.: Hyaluronic acid and rheumatic diseases, Mod. Concepts Cardiovas. Dis. 17: [n.p.] (Feb.) 1948.
- 1378. Meyer, K., and Ragan, C.: The antirheumatic effect of sodium gentisate, Science 108: 280 (Sept.) 1948.
- 1379. Meyer, K., and Rapport, M. M.: Hydrolysis of chondroitin sulfate by testicular hyaluronidase, Arch. Biochem. 27: 287 (July) 1950.
- 1380. Meyer, O.: Inflammatory phlebostenosis as factor in localization of rheumatic diseases, Indust. Med. 15: 197 (Mar.) 1946.
- 1381. Meyer, O.: Phlebological treatment of arthritis of knee, Indust. Med. 17: 405 (Oct.)
- 1382. Meyer, O.: Abuse of rest in arthritis, Rheumatism 3: 111 (July-Sept.) 1947.
- 1383. Meyerding, H. W., and Flashman, F. L.: Backache, J. A. M. A. 130: 75 (Jan.) 1946.
- 1384. Meyerding, H. W., and Ivins, J. C.: Causation and treatment of painful stiff shoulder; subdeltoid bursitis, periarthritis, tendinitis and adhesive capsulitis, Arch. Surg. 56: 693 (June) 1948.
- 1385. Miale, J. B.: Characteristic urinary findings in visceral angiitis (periarteritis nodosa, lupus erythematosus), Am. J. Clin. Path. 17: 820 (Oct.) 1947.
- 1386. Miale, J. B., and Singletary, W. V.: Cutaneous manifestations of gonococcic infection; keratosis blennorrhagica treated with penicillin, Arch. Dermat. and Syph. 57: 151 (Feb.) 1948.
- 1387. Miale, J. B.: The manifestations and mechanisms of vascular allergy. A critical review, Ann. Allergy 7: 124 (Jan.-Feb.) 1949.
- 1388. Michael, M., Jr.: The role of tonsillectomy in the management of recurrent streptococcal sore throat, rheumatic fever and glomerulonephritis, Am. J. Med. 6: 462 (Apr.) 1949.
- 1389. Michael, M., Jr., Cole, R. M., Beeson, P. B., and Olson, B. J.: Preliminary report on study of 350 cases with special reference to epidemiology, Am. Rev. Tuberc. 62: 403 (Oct.) 1950.
- 1390. Michele, A. A., Davies, J. J., Krueger, F. J., and Lichtor, J. M.: Scapulocostal syndrome (fatigue-postural paradox), New York State J. Med. 50: 1353 (June) 1950.
- 1391. Michele, A. A., and Krueger, F. J.: Streptomycin and surgery in the treatment of tuberculous joints, New York State J. Med. 48: 1470 (July) 1948.
- 1392. Michelsen, J. J.: Ruptured cervical disks; summary of 24 verified cases, S. Clin. North America 27: 1246 (Oct.) 1947.
- 1393. Milch, H.: Recurrent bilateral ankylosis of the temporomandibular joint, Bull. Hosp. Joint Dis. 8: 45 (Apr.) 1947.
- 1394. Milch, H.: Resection-angulation operation for arthritis of hip, Bull. Hosp. Joint Dis. 9: 187 (Oct.) 1948.

1395. Milch, H.: Extension osteotomy of the femur for spondylitis ankylopoietica, Bull. Hosp. Joint Dis. 10: 64 (Apr.) 1949.

1396. Milch, H.: The resection-angulation operation for arthritis and ankylosis of the hip, J. Internat. Coll. Surgeons 13: 750 (June) 1950.

1397. Milch, H.: The resection-angulation operation for arthritis of the hip, Geriatrics 5: 280 (Sept.-Oct.) 1950.

1398. Miller, C. F.: Occupational calcareous peritendinitis of the feet; a case report, Am. J. Roentgenol. 61: 506 (Apr.) 1949.

1399. Miller, D., and Birsner, J. W.: Coccidioidal granuloma of bone, Am. J. Roentgenol. 62: 229 (Aug.) 1949.

1400. Miller, D., and Vanderfield, G.: Clinico-pathological observations on lumbar intervertebral disk protrusion; account of 53 consecutive cases treated by operation at one centre, M. J. Australia 2: 200 (Aug.) 1947.

1401. Miller, H. G., and Daley, R.: Clinical aspects of polyarteritis nodosa, Quart. J. Med. 15: 255 (Oct.) 1946.

1402. Miller, H. I., and Miller, G. F.: Post-traumatic reflex dystrophies, Am. J. Surg. 79: 814 (June) 1950.

1403. Miller, J.: Allergic arthritis, Ann. Allergy 7: 497 (July-Aug.) 1949.

1404. Miller, J. E., Lynch, E. R., and Lansbury, J.: Failure of sensitized sheep cell agglutination to clarify the diagnosis of rheumatic disease, J. Lab. and Clin. Med. 34: 1216 (Sept.) 1949.

1405. Miller, J. M., Lipin, R. J., and Ginsberg, M.: Streptomycin in the treatment of tuberculous tenosynovitis, J. A. M. A. 142: 408 (Feb.) 1950.

1406. Miller, J. W., Edmunds, L. H., and Armstrong, T. M.: Surgical treatment of low back pain; an end result of 82 cases, Northwest Med. 48: 614 (Sept.) 1949.

1407. Miller, L. F., and Hilkevitch, A.: Osteochondritis dissecans of the shoulder, Am. J. Roentgenol. 63: 223 (Feb.) 1950.

1408. Milles, H. L.: Importance of diet in chronic rheumatism, M. Press 218: 351 (Oct.) 1947.

1409. Mills, E. S.: A case of dermatomyositis, Tr. A. Am. Physicians 60: 118, 1947.

1410. Milzer, A., Kohn, K. H., and MacLean, H.: Oral prophylaxis of rheumatic fever with penicillin; resistant hemolytic streptococci, J. A. M. A. 136: 536 (Feb.) 1948.

1411. Mirsky, I. A.: Artificial induction of subcutaneous nodules in rheumatic fever, Proc. Soc. Exper. Biol. and Med. 60: 143, 1945.

1412. Mitchell, W. R. D.: Injuries round the knee joint, M. Press 217: 303 (Apr.) 1947.

1413. Moersch, H. J.: Pulmonary coccidioidal mycosis; clinical aspects, Proc. Staff Meet., Mayo Clin. 22: 276 (July) 1947.

1414. Moffatt, T. W., Barnes, S. S., and Weiss, R. S.: Induction of L. E. cell (Hargraves) in normal peripheral blood, J. Invest. Dermat. 14: 153 (Mar.) 1950.

1415. Møller, P. F.: Roentgen picture of tabetic arthropathies and affections of bones, Acta radiol. 26: 535, 1945.

1416. Moloney, J. C.: The effort syndrome and low back pain, J. Nerv. and Ment. Dis. 108: 10 (July) 1948.

1417. Montagna, W.: Glycogen and lipids in human cartilage, with some cytochemical observations on the cartilage of the dog, cat, and rabbit, Anat. Rec. 103: 77 (Jan.) 1949.

1418. Montgomery, H., and McCreight, W. G.: Disseminate lupus erythematosus, Arch. Dermat. and Syph. 60: 356 (Sept.) 1949.

1419. Montgomery, M. M.: The use of BAL in the treatment of skin reactions due to gold therapy, Ann. Int. Med. 33: 915 (Oct.) 1950.

1420. Montgomery, H.: Capillary fragility in rheumatic fever, U. S. Nav. M. Bull. 46: 1708 (Nov.) 1946.

1421. Moore, D. H., and Harris, T. N.: Occurrence of hyaluronidase inhibitors in fractions of electrophoretically separated serum, J. Biol. Chem. 179: 377 (May) 1949.

- 1422. Moore, F. J., Ridge, G. J., Huntington, R. W., Hall, E. M., Griffith, G. C., and Knowles, R. G.: Production of acute rheumatic-like heart lesions in mice, Proc. Soc. Exper. Biol. and Med. 65: 102, 1947.
- 1423. Moore, M., Jr.: Skeletal manifestations of Gaucher's disease, Memphis M. J. 21: 132 (Sept.) 1946.
- 1424. Moore, M., Jr., and Clarke, C. L.: Extreme calcinosis interstitialis; report of a case, South. M. J. 43: 861 (Oct.) 1950.
- 1425. Moore, M., Jr., and Coley, B. L.: Bone lesions in Gaucher's disease, J. Tennessee M. A. 40: 101 (Apr.) 1947.
- 1426. Moore, M. L.: Measurement of joint motion; technic of goniometry, Physiotherapy Rev. 29: 256 (June) 1949.
- 1427. Moran, F. T.: Calcinosis; brief review of literature and report of 2 cases, South. M. J. 40: 840 (Oct.) 1947.
- 1428. Morgan, H. R., and Bennett, G. A.: Intra-articular changes induced in rabbits by injection of typhoid somatic antigen, Arch. Path. 44: 609 (Dec.) 1947.
- 1429. Morgan, J., and Comroe, B. I.: Brief review of arthritis and allied conditions in tropical diseases, Ann. Int. Med 24: 233 (Feb.) 1946.
- 1430. Morgan, S. F.: Rheumatic fever control; important pediatric problem, Wisconsin M. J. 46: 792 (Aug.) 1947.
- 1431. Morgans, M. E.: Gaucher's disease without splenomegaly, Lancet 2: 576 (Oct.) 1947.
- 1432. Morris, M. H.: Acute lupus erythematosus disseminata treated with penicillin, New York State J. Med. 46: 917 (Apr.) 1946.
- 1433. Morris, M. H.: Charcot's joint in diabetes mellitus, New York State J. Med. 47: 1395 (June) 1947.
- 1434. Morrison, L. R., Catoggio, P. M., and Bauer, W.: The histopathology of the neuro-muscular system in rheumatoid arthritis, Ann. Rheumat. Dis. 8: 304 (Dec.) 1949.
- 1435. Morrison, L. R., Short, C. L., Ludwig, A. O., and Schwab, R. S.: Neuromuscular system in rheumatoid arthritis; electromyographic and histologic observations, Am. J. M. Sc. 214: 33 (July) 1947.
- 1436. Morrison, R. J. G., and Thompson, M.: Reiter's syndrome; report on 9 cases, Lancet 1: 636 (Apr.) 1948.
- 1437. Morse, R. A., and Greene, J. A.: Haverhill fever (erythema arthriticum epidemicum); report of a case with necropsy observations, Texas State J. Med. 45: 768 (Nov.) 1949.
- 1438. Morton, D. E.: Comparative anatomico-roentgenological study of cervical spine of 20 cadavers, Am. J. Roentgenol. 63: 523 (Apr.) 1950.
- 1439. Morton, D. E.: Anatomical study of human spinal column, with emphasis on degenerative changes in cervical region, Yale J. Biol. and Med. 23: 126 (Nov.) 1950.
- 1440. Moss, L. L., and Toone, E. C., Jr.: The successful treatment of gold dermatitis with British antilewisite; a case report, Virginia M. Monthly 76: 23 (Jan.) 1949.
- 1441. Moss, M. J.: Chronic brucellosis; preliminary report, J. Indiana M. A. 39: 481 (Oct.) 1946.
- 1442. Mossberger, J. I.: Rheumatic pneumonia; report of 2 cases, J. Pediat. 30: 113 (Feb.) 1947.
- 1443. Movitt, E. R., Mackenbrock, F. C., and Clement, C. E.: Periarteritis nodosa; antigens of *Trichinella spiralis* and poison oak as exciting causes, Stanford M. Bull. 8: 59 (May) 1950.
- 1444. Mowbray, R., Latner, A. L., and Middlemiss, J. H.: Ankylosing spondylitis; radiological, clinical, and biochemical investigations in series of cases, Quart. J. Med. 18: 187 (July) 1949.
- 1444a. Moxon, R. K.: Acute disseminated lupus erythematosus in male, with fatal termination in 16 days, U. S. Nav. M. Bull. 48: 286 (Mar.-Apr.) 1948.

1445. Mukherjee, S. K.: Rheumatoid arthritis in infants and children, with unusual manifestations, Indian M. Gaz. 85: 247 (June) 1950.

1446. Muirhead, E. E., Kreissl, L. J., Jr., and Gordon, C. E.: Synovial sarcoma and relatively benign synovioma, Texas J. Med. 45: 202 (Apr.) 1949.

1447. Müller, G. M.: Arthrodesis of trapezio-metacarpal joint for osteoarthritis, J. Bone and Joint Surg. 31B: 540 (Nov.) 1949.

1448. Mulligan, R. M., and Stricker, F. L.: Metastatic calcification produced in dogs by hypervitaminosis D and haliphagia, Am. J. Path. 24: 451 (May) 1948.

1449. Munslow, R. A., and Hinchey, J. J.: Protruded intervertebral disk syndrome; conservatism in management. Texas State J. Med. 46: 24 (Jan.) 1950.

1450. Murphey, F., Pascucci, L. M., Meade, W. H., and Van Zwaluwenburg, B. R.: My-elography in patients with ruptured cervical intervertebral discs, Am. J. Roentgenol. 56: 27 (July) 1946.

1451. Murphy, G. E., and Swift, H. F.: Induction of cardiac lesions, closely resembling those of rheumatic fever, in rabbits following repeated skin infections with group A streptococci, J. Exper. Med. 89: 687 (June) 1949.

1452. Murphy, G. E., and Swift, H. F.: The induction of rheumatic-like cardiac lesions in rabbits by repeated focal infections with group A streptococci; comparison with the cardiac lesions of serum disease, J. Exper. Med. 91: 485 (May) 1950.

1453. Murphy, I. D.: Unusual form of de Quervain's syndrome; report of 2 cases, J. Bone and Joint Surg. 31A: 858 (Oct.) 1949.

1454. Murray, P. D. F., and Kodicek, E.: Bones, muscles and vitamin C; the effect of a partial deficiency of Vitamin C on the repair of bone and muscle in guinea pigs, J. Anat. 83: 158, 1949.

1455. Murrell, T. W., and Murrell, T. W., Jr.: Physician and psoriatic, South. M. J. 40: 355 (Apr.) 1947.

1456. Mussey, R. D., Jr., and Henderson, M. S.: Osteochondromatosis, J. Bone and Joint Surg. 31A: 619 (July) 1949.

1457. Mustard, H. S.: Rheumatic fever in perspective of public health, Am. J. Med. 2: 609 (June) 1947.

1458. Myers, W. K.: Gout, Am. Pract. 3: 158 (Nov.) 1948.

1459. Natenshon, A. L.: Possible recovery from disseminated lupus erythematosus; preliminary report, M. Times 78: 249 (June) 1950.

1460. Nathan, P. W.: On pathogenesis of causalgia in peripheral nerve injuries, Brain 70: 145 (June) 1947.

1460a. National Research Council Final Report, Committee for Survey of Research on Rheumatic Diseases, Washington, D. C., 1949.

1461. Nauta, W. J. H., and Landsmeer, J. M. F.: Gross anatomy of periarticular tissues of shoulder joint, Ann. Rheumat. Dis. 7: 164 (Sept.) 1948.

1462. Neale, A. V.: Polyarteritis in childhood, Arch. Dis. Childhood 24: 224 (Sept.) 1949.

1463. Neligan, A. R.: Palindromic rheumatism, Brit. M. J. 1: 205 (Feb.) 1946.

1464. Nelson, H. G., and Seal, J. R.: Studies on rheumatic fever; comparative value of Weltmann serocoagulation reaction and sedimentation rate (Cutler) in determining activity of rheumatic process, J. Lab. and Clin. Med. 35: 220 (Feb.) 1950.

1465. Neu, H. N.: Pain in the neck and shoulder, Nebraska M. J. 35: 312 (Oct.) 1950.

1466. Neuberger, A.: Studies on alcaptonuria; estimation of homogentisic acid, Biochem. J. 41: 431, 1947.

1467. Neuberger, A., Rimington, C., and Wilson, J. M. G.: Studies on alcaptonuria; investigations on case of human alcaptonuria, Biochem. J. 41: 438, 1947.

1468. Neuberger, A., and Webster, T. A.: Studies on alcaptonuria; experimental alcaptonuria in rats, Biochem. J. 41: 449, 1947.

1469. Neuberger, K. T.: Brain in rheumatic fever, Dis. Nerv. System 8: 259 (Aug.) 1947.

- 1470. Neudorff, L. G.: Chrysotherapy in rheumatoid arthritis, J. Missouri M. A. 47: 172 (Mar.) 1950.
- 1471. Neuman, R. E., and Tytell, A. A.: Action of proteolytic enzymes on collagen, Proc. Soc. Exper. Biol. and Med. 73: 409 (Mar.) 1950.
- 1471a. Neviaser, J. S.: Adhesive capsulitis of the shoulder, American Academy of Orthopedic Surgeons, Instructoral Course Lecture 6: 281, 1949.
- 1472. Newman, L. B.: Exercising device for increasing joint action, Arch. Phys. Med. 26: 762 (Dec.) 1945.
- 1473. Newman, W. H.: Arthrodesis of adult knee, with special reference to Charcot's joints, New Orleans M. and S. J. 103: 20 (July) 1950.
- 1474. Nicholson, J. T.: Pyogenic arthritis with pathologic dislocation of the hip in infants, J. A. M. A. 141: 826 (Nov.) 1949.
- 1475. Niebauer, J. J., and King, D.: Arthrodesis of hip produced by internal fixation, J. Bone and Joint Surg. 28: 103 (Jan.) 1946.
- 1476. Niehus, L.: Marie-Strumpell arthritis; with emphasis on physical therapy regime, Physiotherapy Rev. 29: 350 (Aug.) 1949.
- 1477. Nisbet, B. R.: Incidence of rheumatism, Ann. Rheumat, Dis. 5: 168 (Sept.) 1946.
- 1478. Nissen, H. A.: Gout; based on 5-year study of 1500 arthritic patients, Journal Lancet 67: 269 (July) 1947.
- 1479. Nissen, H. A.: Continuous follow-up study of 500 arthritics, Journal Lancet 67: 358 (Oct.) 1947.
- 1480. Noble, J. A.: Painful stiff shoulder, Nova Scotia M. Bull. 28: 141 (June) 1949.
- 1481. Nohteri, H.: Case of peritenonitis calcificans et ossificans in unusual location, J. Internat. Coll. Surgeons 9: 712 (Nov.-Dec.) 1946.
- 1482. Norcross, B. M., Robins, H. M., and Lockie, L. M.: D-tubocurarine in oil-wax suspension in rheumatoid spondylitis, J. A. M. A. 140: 397 (May) 1949.
- 1483. Norgaard, A.: Chronic polyarthritis in Denmark, Acta med. Scandinav. (supp. 206) 130: 437, 1948.
- 1484. Norley, T., and Bickel, W. H.: Calcification of the bursae of the knee, J. Bone and Joint Surg. 31A: 417 (Apr.) 1949.
- 1485. Norman, C. F.: Vitamin D therapy in the treatment of scleroderma and allied conditions; three cases, Geriatrics 2: 24 (Jan.-Feb.) 1947.
- 1486. Nørregaard, S.: A case of dermatomyositis with universal calcinosis, Acta dermatvenereol. 27: 479, 1947.
- 1487. Norris, D. C.: Studies in incidence of rheumatism among industrial and clerical workers, Brit. J. Phys. Med. 9: 70 (May-June) 1946.
- 1488. Northrop, P. M.: Temporomandibular ankylosis; report of a case, J. Oral Surg. 5: 256 (July) 1947.
- 1489. Norwich, I.: Calcification of supraspinatus tendon; infiltration therapy with local (procaine hydrochloride) anesthesia and multiple needling, Surg., Gynec. and Obst. 86: 183 (Feb.) 1948.
- 1490. Nutting, G. C., and Borasky, R.: Electron microscopy of collagen, Am. Leather Chemists' Assoc. J. 43: 96, 1948.
- 1491. Ober, F. R.: Physical medicine and lame back, J. A. M. A. 137: 133 (May) 1948.
- 1492. Obletz, B. E., Lockie, L. M., Milch, E., and Hyman, I.: Early effects of partial sensory denervation of the hip for relief of pain in chronic arthritis, J. Bone and Joint Surg. 31A: 805 (Oct.) 1949.
- 1493. O'Connell, J. E. A.: Indications for and results of excision of lumbar intervertebral disc protrusions: review of 500 cases; Hunterian lecture, Ann. Roy. Coll. Surgeons, England 6: 403 (June) 1950.
- 1494. O'Connell, W. J., and Burns, F. J.: Cortisone therapy in rheumatoid arthritis, Rhode Island M. J. 33: 289 (June) 1950.

1495. Odell, R. T., Ramsey, R. H., and Key, J. A.: Results after operative removal of intervertebral discs. South. M. J. 43: 759 (Sept.) 1950.

1497. O'Donoghue, A. F., Donohue, E. S., and Zimmerman, W. W.: Bilateral osteochondritis of tarsal navicular and first cuneiform; case report, J. Bone and Joint Surg. 30A: 780 (July) 1948.

1498. Ogryzlo, M. A.: Chronic inflammatory lesions of skeletal muscle in rheumatoid arthritis and in other diseases. Arch. Path. 46: 301 (Oct.) 1948.

1499. Ogryzlo, M. A., and Graham, W.: Reiter's syndrome: Effect of pituitary adrenocorticotropic hormone (ACTH) and cortisone, J. A. M. A. 144: 1239 (Dec.) 1950.

1500. Ogston, A. G., and Stanier, J. E.: On state of hyaluronic acid in synovial fluid, Biochem. J. 46: 364 (Mar.) 1950.

1501. Oldberg, E.: Syndrome of protruded intervertebral disk, M. Clin. North America 32: 1403 (Sept.) 1948.

1502. Oldberg, S.: On etiology of Heberden's nodes, preliminary report, Acta med. Scandinav., supp. 170: 381, 1946.

1503. O'Leary, P. A.: Dermatomyositis, M. Clin. North America 33: 21 (Jan.) 1949.

1504. O'Leary, P. A., and Farber, E. M.: Evaluation of beta-dimethylaminoethyl benzhydryl ether hydrochloride (benadryl) in treatment of urticaria, scleroderma and allied disturbances, Proc. Staff Meet., Mayo Clin. 21: 295 (Aug.) 1946.

1505. Olenick, E. J., and Sargent, J. W.: Urologic and ophthalmologic observations in 2 cases of Reiter's syndrome, U. S. Nav. M. Bull. 47: 657 (July-Aug.) 1947.

1506. Olin, H. A.: Subacromial bursitis; clinical and roentgen observations, Radiology 47: 593 (Dec.) 1946.

1507. Oppel, T. W., Coker, C., and Milhorat, A. T.: Effect of pituitary adrenocorticotropin (ACTH) in dermatomyositis, Ann. Int. Med. 32: 318 (Feb.) 1950.

1508. Oppenheim, A., and Pollack, R. S.: Boeck's sarcoid (sarcoidosis), Am. J. Roentgenol. 57: 28 (Jan.) 1947.

1509. Opsahl, J. C.: The influence of hormones from the adrenal cortex on the dermal spread of India ink with and without hyaluronidase; preliminary report, Yale J. Biol. and Med. 21: 255 (Jan.) 1949.

1510. Opsahl, J. C.: Dermal spreading of India ink with and without hyaluronidase as influenced by hormones from the adrenal cortex, Yale J. Biol. and Med. 21: 487 (July) 1949.

 Opsahl, J. C.: Role of certain steroids in the adrenal-hyaluronidase relationship, Yale J. Biol. and Med. 22: 115 (Dec.) 1949.

1512. Oren, H.: Gold salts in treatment of rheumatoid arthritis; report on 150 additional cases, M. Rec. 159: 420 (July) 1946.

1513. Orr, H.: Acute disseminated lupus erythematosus, Canad. M. A. J. 62: 432 (May) 1950.

1514. Orr, L. M., Mathers, F., and Butt, T. C.: Somatic pain due to fibrolipomatous nodules, simulating uretero-renal disease: a preliminary report, J. Urol. 59: 1061 (June) 1948.

1515. Osborne, G. V., and Fahrni, W. H.: Oblique displacement osteotomy for osteoarthritis of the hip joint. J. Bone and Joint Surg. 32B: 148 (May) 1950.

1516. Ott, V.: Present Swiss concepts of rheumatism and physical medicine, Ann. Rheumat. Dis. 5: 206 (Dec.) 1946.

1517. Overton, L. M.: Degenerative changes in cervical spine as common cause of shoulder and arm pain, South. Surgeon 16: 599 (June) 1950.

1518. Pack, G. T., and Ariel, I. M.: Sarcoma (malignant synovioma); report of 60 cases, Surgery 28: 1047 (Dec.) 1950.

1519. Padgett, E. C., Robinson, D. W., and Stephenson, K. L.: Temporomandibular joint, Surgery 24: 426 (Aug.) 1948.

1520. Pagel, W., Woolf, A. L., and Asher, R.: Histologic observations on dermatomyositis, J. Path. and Bact. 61: 403 (July) 1949.

- 1521. Palik, E., and Schenken, J. R.: Disseminated granuloma venereum, Am. J. Clin. Path. 15: 419 (Oct.) 1945.
- 1522. Pappenheimer, A. M., Daniels, J. B., Cheever, F. S., and Weller, T. H.: Lesions caused in suckling mice by certain viruses isolated from cases of so-called nonparalytic poliomyelitis and of pleurodynia, J. Exper. Med. 92: 169 (Aug.) 1950.
- 1523. Pardee, H. E. B.: Electrocardiographic findings in rheumatic heart disease, Am. J. Med. 2: 528 (May) 1947.
- 1524. Pardee, M. L.: Synovectomy of the knee joint; a review of the literature and presentation of cases, J. Bone and Joint Surg. 30A: 908 (Oct.) 1948.
- 1525. Parker, D.: Sacro-iliac tuberculous arthritis, M. J. Australia 2: 319 (Aug.) 1950.
- 1526. Parker, H. L., and Kernohan, J. W.: The central nervous system in periarteritis nodosa, Proc. Staff Meet., Mayo Clin. 24: 43 (Jan.) 1949.
- 1527. Parker, J. M., and Modlin, J. J.: Compound injuries of the knee joint; treatment of noninfected knee joints, Ann. Surg. 125: 341 (Mar.) 1947.
- 1528. Parkhurst, G. E., Harb, F. W., and Cannefax, G. R.: "Penicillin-resistant gonorrhea" vs. "non-specific urethritis," J. Ven. Dis. Inform. 28: 211 (Oct.) 1947.
- 1529. Parks, J., and Fraser, C. K.: Lymphogranuloma venereum, Am. Pract. 1: 371 (Mar.) 1947.
- 1530. Paronen, I.: Reiter's disease; study of 344 cases observed in Finland, Acta med. Scandinav. (supp. 212) 131: 1, 1948.
- 1531. Parr, L. J. A., and Shipton, E.: Spondylitis ankylopoietica, M. J. Australia 1: 277 (Mar.) 1946.
- 1532. Parr, L. J. A., and Shipton, E. A.: Basophilic stippling of red corpuscles with special reference to its occurrence during chrysotherapy, M. J. Australia 1: 193 (Feb.) 1947.
- 1533. Parr, L. J. A., and Shipton, E.: Sulphonamide therapy in rheumatoid arthritis, Rheumatism 5: 25 (Jan.) 1949.
- 1534. Partridge, S. M.: The chemistry of connective tissues. I. The state of combination of chondroitin sulphate in cartilage, Biochem. J. 43: 387, 1948.
- 1535. Patrick, J.: Pin and graft arthrodesis for osteoarthritis of hip, Lancet 2: 9 (July) 1946.
- 1536. Patterson, R. H., and Patterson, R. L.: Operative technic for calcified tendons about the shoulder joint, Am. J. Surg. 78: 582 (Nov.) 1949.
- 1537. Patton, I. J., and Williamson, J. A.: Fibrositis as factor in differential diagnosis of visceral pain, Canad. M. A. J. 58: 162 (Feb.) 1948.
- 1538. Paul, J. R.: Epidemiology of rheumatic fever, Am. J. Med. 2: 66 (Jan.) 1947.
- 1539. Paul, L.: Psychosomatic aspects of low back pain; review of recent articles, Psychosom. Med. 12: 116 (Mar.-Apr.) 1950.
- 1540. Paul, L. W., and Moir, W. W.: Roentgen diagnostic aspects of chronic arthritis and bursitis, Radiology 49: 6 (July) 1947.
- 1541. Paul, W. D.: Toxic manifestations of large doses of vitamin D as used in treatment of arthritis, J. Iowa M. Soc. 36: 141 (Apr.) 1946.
- 1542. Paull, R.: Periarteritis nodosa (panarteritis nodosa) with report of 4 proven cases, California Med. 67: 309 (Nov.) 1947.
- 1543. Peacher, W. G., and Robertson, R. C. L.: Absorption of pantopaque following myelography, Radiology 47: 186 (Aug.) 1946.
- 1544. Peale, A. R., Gildersleeve, N., and Lucchesi, P. F.: Periarteritis nodosa complicating scarlet fever, Am. J. Dis. Child. 72: 310 (Sept.) 1946.
- 1545. Pearce, R. H., and Watson, E. M.: The mucopolysaccharides of human skin, Canad. J. Research 27: 43 (Feb.) 1949.
- 1546. Pearse, A. G. E.: The hypophysis in rheumatoid arthritis, Lancet 1: 954 (May) 1950.
- 1547. Pease, C. N.: Fusion of the hip in children; Chandler method, J. Bone and Joint Surg. 29: 874 (Oct.) 1947.
- 1548. Pelland, P. O., and Hoffman, W.: Operative treatment of acute subdeltoid bursitis with calcification, M. Ann. District of Columbia 17: 371 (July) 1948.

1549. Pemberton, R.: Treatment of arthritis, Pennsylvania M. J. 52: 712 (Apr.) 1949.

1550. Pemberton, R., Eiman, J., Patterson, F. M. S., and Stackhous, E. A.: Attempts at experimental production of arthritis, J. Lab. and Clin. Med. 32: 1121 (Sept.) 1947.

1551. Perera, G. A., and Ragan, C.: Hypoadrenalism: steroidal mediation of sodium action on blood pressure; modification of antiarthritic response to cortisone, Proc. Soc. Exper. Biol. and Med. 75: 99 (Oct.) 1950.

1552. Perera, G. A., and Plotz, C. M.: The response to methacholine in rheumatoid arthritis, Am. J. M. Sc. 220: 307 (Sept.) 1950.

1553. Perl, A. F.: Palindromic rheumatism, Canad. M. A. J. 57: 382 (Oct.) 1947.

1554. Perlman, H. H.: Undecylenic acid by mouth in the treatment of arthritis and bursitis; a preliminary report, Urol. and Cutan. Rev. 53: 103 (Feb.) 1949.

1555. Pernworth, P.: Causalgia, Indust. Med. 16: 525 (Nov.) 1947.

1556. Perrigard, G. E.: Supernumerary bursa of pectineus muscle simulating hernia in inguinal region, Brit. J. Surg. 34: 314 (Jan.) 1947.

1557. Persons, E. L.: Basis for treatment of rheumatoid arthritis, North Carolina M. J. 8: 131 (Mar.) 1947.

1558. Persons, E. L.: Medical aspects of chronic joint disease, Nebraska M. J. 34; 90 (Mar.) 1949.

1559. Peterman, E. A.: Glucuronic acid deficiency in the rheumatic diseases, Journal Lancet 67: 451 (Dec.) 1947.

1560. Peters, J. H.: Reiter's syndrome with keratotic dermatitis; report of a case, Arch. Dermat. and Syph. 59: 217 (Feb.) 1949.

1561. Petersen, J.: A case of osseous changes in a patient with hemophilia, Acta radiol. 28: 323, 1947.

 Peterson, H. O.: Value of x-ray examination in diagnosis of ruptured intervertebral disc, Minnesota Med. 29: 904 (Sept.) 1946.

1563. Peterson, J. C., and Bishop, L. K.: Treatment of serum sickness with benadryl, J. A. M. A. 133: 1277 (Apr.) 1947.

1564. Peyton, W. T., and Simmons, D. R.: Herniated intervertebral disk; analysis of 90 cases, Arch. Surg. 55: 271 (Sept.) 1947.

1565. Phalen, G. S.: The diagnosis and treatment of "mechanical backache," J. A. M. A. 141: 445 (Oct.) 1949.

1566. Phemister, D. B.: Lesions of bones and joints arising from interruption of the circulation, J. Mt. Sinai Hosp. 15: 55 (July-Aug.) 1948.

1567. Phillips, K.: Clinical response to Crowe's vaccine in 125 cases of rheumatic disease, J. Florida M. A. 36: 290 (Nov.) 1949.

1568. Pickard, N. S.: Rheumatoid arthritis in children; clinical study, Arch. Int. Med. 80: 771 (Dec.) 1947.

1569. Pickering, G. W.: Significance of the discovery of the effects of cortisone on rheumatoid arthritis, Lancet 2: 81 (July) 1950.

1570. Pickles, W. N.: The country doctor, Lancet 1: 201 (Feb.) 1948.

1571. Pike, M. M.: Legg-Perthes disease; a method of conservative treatment, J. Bone and Joint Surg. 32A: 663 (July) 1950.

1572. Pike, R. M.: Streptococcal hyaluronic acid and hyaluronidase; production and subsequent destruction of hyaluronic acid by certain strains of group A streptococci, J. Infect. Dis. 83: 12 (July-Aug.) 1948.

1573. Pike, R. M.: The production of hyaluronic acid and hyaluronidase by strains of group A streptococci, Ann. New York Acad. Sc. 52: 1070 (May) 1950.

1574. Pike, R. M., Sulkin, S. E., and Coggeshall, H. C.: Serologic reactions in rheumatoid arthritis; concerning the nature of the factor in rheumatoid arthritis serum responsible for increased agglutination of sensitized sheep erythrocytes, J. Immunol. 63: 447 (Dec.) 1949.

1575. Pinck, B. D.: Reiter's syndrome, Am. J. M. Sc. 214: 76 (July) 1947.

- 1576. Pipkin, G.: Symposium on prognosis; prognosis on sprains, J. Insur. Med. 4: 17 (June-Aug.) 1949.
- 1577. Pirani, C. L., Bly, C. G., and Sutherland, K.: Scorbutic arthropathy in the guinea pig, Arch. Path. 49: 710 (June) 1950.
- 1578. Platt, H.: The backache-sciatica syndrome and the intervertebral disc, Rheumatism 4: 218 (Oct.) 1948.
- 1579. Plenk, H. P.: Psoriatic arthritis; report of case, Am. J. Roentgenol. 64: 635 (Oct.) 1950.
- 1580. Plotz, C. M., Blunt, J. W., Jr., and Ragan, C.: Effect of pituitary adrenocorticotropic hormone (ACTH) on disseminated lupus erythematosus, Arch. Dermat. and Syph. 61: 913 (June) 1950.
- 1581. Plotz, C. M., Howes, E. L., Blunt, J. W., Meyer, K., and Ragan, C.: Action of cortisone on mesenchymal tissues, Arch. Dermat. and Syph. 61: 919 (June) 1950.
- 1582. Pohle, E. A., and Morton, J. A.: Roentgen therapy in arthritis, bursitis, and allied conditions, Radiology 49: 19 (July) 1947.
- 1583. Pohle, E. A., and Tomlinson, C.: Roentgen therapy in traumatic myositis ossificans, Am. J. M. Sc. 215: 372 (Apr.) 1948.
- 1584. Pokress, M. J., and Goldberger, E.: Study of the Q-T interval in rheumatic fever, Am. Heart J. 38: 423 (Sept.) 1949.
- 1585. Polley, H. F.: Physical medicine in the care of rheumatoid arthritis, South. M. J. 40: 596 (July) 1947.
- 1586. Polley, H. F.: Transfusions of blood from pregnant women for rheumatoid arthritis, J. A. M. A. 139: 718 (Mar.) 1949.
- 1587. Polley, H. F., and Mason, H. L.: Rheumatoid arthritis; effects of certain steroids other than cortisone and of some adrenal cortex extracts, J. A. M. A. 143: 1474 (Aug.) 1950.
- 1588. Polley, H. F., and Slocumb, C. H.: Rheumatoid spondylitis; a study of 1,035 cases, Ann. Int. Med. 26: 240 (Feb.) 1947.
- 1589. Ponseti, I.: Evolution and treatment of tuberculosis of the hip, Surg., Gynec. and Obst. 87: 257 (Sept.) 1948.
- 1590. Poore, G. C.: Progress in the treatment of gonorrhea, J. Maine M. A. 37: 185 (July) 1946.
- 1591. Porteous, W. M.: Arthritis in poliomyelitis; report of a case, New Zealand M. J. 45: 441 (Oct.) 1946.
- 1592. Porter, J. E., and Foster, T. A.: Rat-bite fever, J. Maine M. A. 37: 93 (Apr.) 1946.
- 1593. Porter, K. R., and Vanamee, P.: Observations on the formation of connective tissue fibers, Proc. Soc. Exper. Biol. and Med. 71: 513, 1949.
- 1594. Posch, J. L., and Stofer, B. E.: Case of snapping thumb, J. Michigan M. Soc. 46: 1181 (Oct.) 1947.
- 1595. Post, C. F., and Sheads, C., Jr.: A case of yaws in New York City, New York State J. Med. 48: 1920 (Sept.) 1948.
- 1596. Potter, T. A.: Rheumatoid spondylitis (Strümpell-Marie arthritis); orthopedic management, Am. Pract. and Digest Treat. 1: 1129 (Nov.) 1950.
- 1597. Powell, H. M., Jamieson, W. A., and Rice, R. M.: Effectiveness of streptomycin in arthritis of rats, Proc. Soc. Exper. Biol. and Med. 62: 8 (May) 1946.
- 1598. Power, F. K., and Lancefield, S. M.: Lupus erythematosus disseminatus, Northwest Med. 49: 269, 1950.
- 1599. Praetorius, E., and Kirk, J. E.: Hypouricemia: with evidence for tubular elimination of uric acid, J. Lab. and Clin. Med. 35: 865 (June) 1950.
- 1600. Pretty, H. G.: Role of sympathetic nervous system in traumatic surgery as applied to fractures, causalgias and amputation stumps, Am. J. Surg. 74: 527 (Nov.) 1947.
- 1602. Prouty, M., and Schafer, E. L.: Periarteritis nodosa associated with ratbite fever due

to Streptobacillus moniliformis (erythema arthriticum epidemicum), J. Pediat. 36: 605 (May) 1950.

1603. Prunty, F. T. G.: Techniques for the evaluation of adrenal cortical function by use of adrenocorticotrophin: a review, J. Clin. Path. 3: 87 (May) 1950.

1603a. Pugh, D. G.: Roentgenologic manifestations of scleroderma, Am. J. M. Sc. 216: 571, 1948.

1603b. Pugh, D. G.: Rheumatoid spondylitis, Am. J. M. Sc. 214: 568 (Nov.) 1947.

1604. Pund, E. R., and Dick, F., Jr.: Lymphogranuloma venereum; pathologic basis for its various manifestations, Urol. and Cutan. Rev. 51: 345 (June) 1947.

1605. Query, R. Z., Jr.: Rheumatoid spondylitis; its early diagnostic features and management, J. A. M. A. 139: 692 (Mar.) 1949.

1606. Quigley, T. B.: Treatment of contusions, strains and sprains, Ann. West. Med. and Surg. 4: 613 (Oct.) 1950.

1607. Quinn, R. W.: Incidence of rheumatic fever and heart disease in school children in Dublin, Georgia, with some epidemiological and sociological observations, Am. Heart J. 32: 234 (Aug.) 1946.

1608. Quinn, R. W.: Epidemiologic study of 757 cases of rheumatic fever, Arch. Int. Med. 80: 709 (Dec.) 1947.

1609. Quinn, R. W.: Antihyaluronidase studies of sera from patients with rheumatic fever, streptococcal infections, and miscellaneous non-streptococcal diseases, J. Clin. Investigation 27: 471 (July) 1948.

1610. Quinn, R. W.: The antihyaluronidase content of human blood serum; a study in age differences, J. Immunol. 61: 185 (Feb.) 1949.

1611. Quinn, R. W.: The antihyaluronidase content of blood serum; a study of sera from patients with rheumatic fever, streptococcal infection, miscellaneous nonstreptococcal diseases, and from normal individuals of different ages, Ann. New York Acad. Sc. 52: 1118 (May) 1950.

1612. Quinn, R. W., and Liao, S. J.: A comparative study of antihyaluronidase, antistreptolysin "O," antistreptokinase, and streptococcal agglutination titers in patients with rheumatic fever, acute hemolytic streptococcal infections, rheumatoid arthritis and non-rheumatoid forms of arthritis, J. Clin. Investigation 29: 1156 (Sept.) 1950.

1613. Quinn, R. W., Liao, S. J., and Quinn, J. P.: An environmental and sociological study of rheumatic heart disease: in school children from four Connecticut communities, Am. J. Pub. Health 40: 1285 (Oct.) 1950.

1614. Quintin, T. J., and White, A. R. V.: Reiter's disease, Canad. M. A. J. 58: 191 (Feb.) 1948.

1615. Quiring, D. P., and Boroush, E. L.: Functional anatomy of shoulder girdle, Arch. Phys. Med. 27: 90 (Feb.) 1946.

1616. Raaf, J., and Berglund, G.: Results of operations for lumbar protruded intervertebral disc, J. Neurosurg. 6: 160 (Mar.) 1949.

1617. Race, J.: Plasma viscosity and suspension stability in chronic rheumatic diseases, Ann. Rheumat. Dis. 7: 239 (Dec.) 1948.

1618. Rae, J.: Report of case of calcinosis cutis associated with Raynaud's disease, M. J. Australia 2: 336 (Aug.) 1950.

1619. Rafsky, H. A., and Herzig, W.: Scleroderma with oesophageal symptoms; report of 2 cases, Gastroenterology 6: 35 (Jan.) 1946.

1620. Ragan, C.: Viscosity of normal human synovial fluid, Proc. Soc. Exper. Biol. and Med. 63: 572 (Dec.) 1946.

1621. Ragan, C.: The general management of rheumatoid arthritis, J. A. M. A. 141: 124 (Sept.) 1949.

1622. Ragan, C.: The effect of adrenocorticotrophic hormone (ACTH) (Armour) on the clinical syndrome of dermatomyositis, Proc., First Clinical ACTH Conference, 1950, The Blakiston Co., Philadelphia, p. 423.

- 1623. Ragan, C.: Undesirable side-effects, withdrawal symptoms and contraindications of the use of cortisone and ACTH in rheumatic diseases, Bull. Rheumat. Dis. 1: 5 (Nov.) 1950.
- 1624. Ragan, C., and Boots, R. H.: Medical progress; rheumatoid arthritis; essentials in management of patients, New York Med. (no. 7) 2: 21 (Apr.) 1946.
- 1625. Ragan, C., and Boots, R. H.: Treatment of gold dermatitides; use of BAL (2,3-dimercaptopropanol), J. A. M. A. 133: 752 (Mar.) 1947.
- 1626. Ragan, C., Donlan, C. P., Coss, J. A., Jr., and Grubin, A. F.: Effects of x-ray irradiation on viscosity of synovial fluid, Proc. Soc. Exper. Biol. and Med. 66: 170 (Oct.) 1947
- 1627. Ragan, C., Grokoest, A. W., and Boots, R. H.: Effect of adrenocorticotrophic hormone (ACTH) on rheumatoid arthritis, Am. J. Med. 7: 741 (Dec.) 1949.
- 1628. Ragan, C., Howes, E. L., Plotz, C. M., Meyer, K., and Blunt, J. W.: Effects of cortisone on production of granulation tissue in the rabbit, Proc. Soc. Exper. Biol. and Med. 72: 718 (Dec.) 1949.
- 1629. Ragan, C., Howes, E. L., Plotz, C. M., Meyer, K., Blunt, J. W., and Lattes, R.: The effect of ACTH and cortisone on connective tissue, Bull. New York Acad. Med. 26: 251 (Apr.) 1950.
- 1630. Ragan, C., and Meyer, K.: The hyaluronic acid of synovial fluid in rheumatoid arthritis, J. Clin. Investigation 28: 56 (Jan.) 1949.
- 1631. Ragan, C., and Meyer, K.: Hyaluronidase and the rheumatic diseases, Ann. New York Acad. Sc. 52: 1108 (May) 1950.
- 1632. Ragan, C., and Tyson, T. L.: Chrysotherapy in rheumatoid arthritis; 3-year study of 142 cases, Am. J. Med. 1: 252 (Sept.) 1946.
- 1633. Rainey, J. F.: Meningococcemia, J. South Carolina M. A. 43: 5 (Jan.) 1947.
- 1634. Rakofsky, M., and Knickerbocker, T. W.: Roentgenological manifestations of primary pulmonary coccidioidomycosis, Am. J. Roentgenol. 56: 141 (Aug.) 1946.
- 1635. Ralston, D. E., and Kvale, W. F.: The renal lesions of periarteritis nodosa, Proc. Staff Meet., Mayo Clin. 24: 18 (Jan.) 1949.
- 1636. Randløv-Madsen, A.: Experimental investigations into the aetiology of Calve-Perthes disease, Acta orthop. Scandinav. 19: 6, 1949.
- 1637. Raney, A. A., and Raney, R. B.: Headache; common symptoms of cervical disk lesions; report of cases, Arch. Neurol. and Psychiat. 59: 603 (May) 1948.
- 1638. Raney, R. B.: Progress in orthopedic surgery for 1946; XI. conditions involving the lower part of the back, Arch. Surg. 58: 352 (Mar.) 1949.
- 1639. Raney, R. B., and Raney, A. A.: Consideration of etiology in development of ruptured intervertebral disc, California Med. 68: 65 (Feb.) 1948.
- 1640. Rapoport, S., and Guest, G. M.: Effect of salicylate on plasma fibrinogen and sedimentation rate in rheumatic and non-rheumatic patients, Proc. Soc. Exper. Biol. and Med. 61: 43 (Jan.) 1946.
- 1641. Rapport, M. M., Meyer, K., and Linker, A.: Correlation of reductimetric and turbidimetric methods for hyaluronidase assay, J. Biol. Chem. 186: 615 (Oct.) 1950.
- 1642. Ratz, R. G.: The general practitioner and rheumatic disease, Canad. M. A. J. 60: 490 (May) 1949.
- 1643. Rau, L.: Subpleural fibroma with hypertrophic osteoarthropathy, Proc. Roy. Soc. Med. 42: 103 (Feb.) 1949.
- 1644. Raven, R. W., Weber, F. P., and Price, L. W.: The necrobiotic nodules of rheumatoid arthritis: case in which the scalp, abdominal wall (involving striped muscle), larynx, pericardium (involving myocardium), pleurae (involving lungs) and peritoneum were affected, Ann. Rheumat. Dis. 7: 63 (June) 1948.
- 1645. Rawls, W. B.: Medical progress; evaluation of present-day therapy in rheumatoid arthritis, New York Med. (no. 15) 3: 19 (Aug.) 1947.
- 1646. Rawls, W. B.: Arthritis and compensation medicine, Compens. Med. 3: 39 (June) 1950.

1647. Ray, B. S.: Differential diagnosis between ruptured lumbar intervertebral disk and certain diseases of spinal and peripheral nervous systems, S. Clin. North America 26: 272 (Apr.) 1946.

1648. Ray, R. B., and Coughlin, E. J., Jr.: Osteochondritis dissecans of talus, J. Bone and Joint Surg. 29: 697 (July) 1947.

1649. Rebuck, J. W., and Berman, L.: Experimental production of the L. E. phenomenon in skin of man, Proc. Soc. Exper. Biol. and Med. 75: 259 (Oct.) 1950.

1650. Recant, L., Hume, D. M., Forsham, P. H., and Thorn, G. W.: Studies on the effect of epinephrine on the pituitary-adrenocortical system, J. Clin. Endocrinol. 10: 187 (Feb.) 1950.

1651. Recant, L., Ott, W. H., and Fischel, E. E.: The antipyretic effect of cortisone, Proc. Soc. Exper. Biol. and Med. 75: 264, 1950.

1652. Reed, C. I.: Vitamin D and tissue calcification, Am. Pract. and Digest Treat. 1: 164 (Feb.) 1950.

1653. Reed, C. I., Joffe, H., and Joseph, N. R.: Autonomic control of synovial-fluid reaction, J. Bone and Joint Surg. 29: 370 (Apr.) 1947.

1654. Reeves, J. E.: Intermittent hydrarthrosis—2 cases, California Med. 71: 359 (Nov.) 1949.

1655. Reich, N. E.: The use of large doses of progesterone in rheumatoid arthritis, Am. Pract. 4: 1 (Sept.) 1949.

1656. Reich, N. E., and Reinhart, J. B.: Dermatomyositis associated with hypertrichosis, Arch. Dermat. and Syph. 57: 725 (Apr.) 1948.

1657. Reid, J.: Does sodium salicylate cure rheumatic fever? Quart. J. Med. 17: 139 (Apr.) 1948.

1658. Reid, J., Watson, R. D., and Sproull, D. H.: Mode of action of salicylate in acute rheumatic fever, Quart. J. Med. 19:1 (Jan.) 1950.

1659. Reidy, J. P.: Measurement of joint ranges; suggestions for simplicity, Brit. J. Plastic Surg. 2: 32 (Apr.) 1949.

1660. Reifenstein, E. C., Jr., and Albright, F.: The metabolic effects of steroid hormones in osteoporosis, J. Clin. Investigation 26: 24 (Jan.) 1947.

1661. Reimann, H. A.: Periodic disease; probable syndrome including periodic fever, benign paroxysmal peritonitis, cyclic neutropenia and intermittent arthralgia, J. A. M. A. 136: 239 (Jan.) 1948.

1662. Rein, C. R., Kitchen, D. K., and Petrus, E. A.: Repository penicillin therapy of yaws in Haitian peasants; clinical and serologic survey, J. Invest. Dermat. 14: 239 (Apr.) 1950.

1663. Rein, C. R., and Kostant, G. H.: Lupus erythematosus: serologic and chemical aspects, Arch. Dermat. and Syph. 61: 898 (June) 1950.

1664. Rein, C. R., Sternberg, J. H., Dwinelle, J. A., and Sheldon, A. J.: Penicillin therapy in yaws and serologic results, Arch. Dermat. and Syph. 57: 942 (June) 1948.

1665. Reiner, M.: Effect of cortisone and adrenocorticotropin therapy on serum proteins in disseminated lupus erythematosus, Proc. Soc. Exper. Biol. and Med. 74: 529 (July) 1950.

1666. Reisner, E. H., Lapin, L., and Steinbrocker, O.: Eosinophilia during intensive gold therapy, New England J. Med. 240: 881 (June) 1949.

 Rennie, J. B., and Fraser, T. N.: Transmission of acute infective hepatitis; therapeutic effect on rheumatoid arthritis, Glasgow M. J. 27: 157 (June) 1946.

1668. Renshaw, A.: Intestinal extract in rheumatic diseases, Ann. Rheumat. Dis. 6: 15 (Mar.) 1947.

1669. Reuter, F. L.: Rat-bite fever, U. S. Nav. M. Bull. 47: 333 (Mar.-Apr.) 1947.

1670. Rhinehart, W. J., and Bauer, J. T.: Disseminated granuloma inguinale of bones, Am J. Roentgenol. 57: 562 (May) 1947.

1671. Rhodes, R. L.: Tenosynovitis of forearm, Am. J. Surg. 73: 248 (Feb.) 1947.

- 1672. Rice, D. V.: The treatment of fibrositis by physiotherapy, 1948, Modern Treatment Yearbook (1 vol.), C. P. G. Wakeley, Editor, Bailliere, London, p. 294.
- 1673. Rice, R. M., Browning, J. S., and Powell, H. M.: Ineffective use of streptomycin in rheumatoid arthritis, Am. J. M. Sc. 214: 64 (July) 1947.
- 1674. Rich, A. R.: Hypersensitivity in disease with especial reference to periarteritis nodosa, rheumatic fever, disseminated lupus erythematosus and rheumatoid arthritis, Harvey Lectures (1946-1947) 42: 106, 1947.
- 1675. Rich, A. R., Berthrong, M., and Bennett, I. L., Jr.: Effect of cortisone upon experimental cardiovascular and renal lesions produced by anaphylactic hypersensitivity, Bull. Johns Hopkins Hosp. 87: 549 (Dec.) 1950.
- 1676. Rich, A. R., and Gregory, J. E.: Experimental anaphylactic lesions of coronary arteries of "sclerotic" type, commonly associated with rheumatic fever and disseminated lupus erythematosus, Bull. Johns Hopkins Hosp. 81: 312 (Nov.) 1947.
- 1677. Richman, R. M., and Barnes, K. O.: Acute instability of the ligaments of the knee as a result of injuries to parachutists, J. Bone and Joint Surg. 28: 473 (July) 1946.
- 1678. Ricker, W., and Clark, M.: Sarcoidosis; clinicopathologic review of 300 cases, including 22 autopsies, Am. J. Clin. Path. 19: 725 (Aug.) 1949.
- 1679. Riddell, A. G.: The treatment of suppurative arthritis of the interphalangeal and metacarpophalangeal joints, Brit. J. Surg. 37: 317 (Jan.) 1950.
- 1680. Riley, E. A.: Boeck's sarcoid; review based upon clinical study of 52 cases, Am. Rev. Tuberc. 62: 231 (Sept.) 1950.
- 1681. Rinehart, J. F.: Observations on treatment of rheumatic fever with vitamin P, Ann. Rheumat. Dis. 5: 11 (Sept.) 1945.
- 1682. Ringrose, E. J., Nowlan, F. B., and Perry, H.: Ehlers-Danlos syndrome; report of a case, Arch. Dermat. and Syph. 62: 443 (Sept.) 1950.
- 1683. Rittwagen, M., Romano, F. J., and Svigals, M. P.: Study of incidence of allergy in children with rheumatic fever, Arch. Pediat. 63: 639 (Dec.) 1946.
- 1684. Robbins, J. V.: Supraspinatus tendonitis calcarea, New York State J. Med. 49: 389 (Feb.) 1949.
- 1685. Roberts, N., and Hughes, R.: Osteochondritis dissecans of elbow joint; clinical study, J. Bone and Joint Surg. 32B: 348 (Aug.) 1950.
- 1686. Roberts, R. A.: De-ossification in lumbar transverse process, Brit. J. Radiol. 22: 540 (Sept.) 1949.
- 1687. Robertson, H. F., Schmidt, R. E., and Feiring, W.: Therapeutic value of early physical activity in rheumatic fever; preliminary report, Am. J. M. Sc. 211: 67 (Jan.) 1946.
- 1688. Robertson, H. F., and Schlamowitz, S. T.: Rheumatic nephritis, Ann. Int. Med. 33: 708 (Sept.) 1950.
- 1689. Robinson, A.: Osteoarthritis of the hip, Canad. M. A. J. 60: 161 (Feb.) 1949.
- 1690. Robinson, D.: Lauron in rheumatoid arthritis (further report), Canad. M. A. J. 55: 162 (Aug.) 1946.
- 1691. Robinson, D.: Roentgen therapy for bursitis of the shoulder, J. M. A. Georgia 39: 205 (May) 1950.
- 1692. Robinson, D.: Rheumatoid arthritis, Canad. M. A. J. 61: 152 (Aug.) 1949.
- 1693. Robinson, D. R.: Pyriformis syndrome in relation to sciatic pain, Am. J. Surg. 73: 355 (Mar.) 1947.
- 1694. Robinson, H. M., Jr., and McCrumb, F. R., Jr.: Comparative analysis of mucocutaneous-ocular syndromes (report of 11 cases and review of literature), Arch. Dermat. and Syph. 61: 539 (Apr.) 1950.
- 1695. Robinson, H. S.: Report on national scheme for treatment of rheumatic disease in Britain, Canad. M. A. J. 56: 665 (June) 1947.
- 1696. Robinson, J. A., Hirsh, H. L., Zeller, W. W., and Dowling, H. F.: Gonococcal arthritis; a study of 202 patients treated with penicillin, sulfonamides or fever therapy, Ann. Int. Med. 30: 1212 (June) 1949.

- 1697. Robinson, J. J., and Currens, J. H.: Preliminary observations on some children with rheumatic heart disease transported to subtropical climate, J. Pediat. 28: 426 (Apr.) 1946.
- 1698. Robinson, R. C. V., and Hahn, R. D.: Sarcoidosis in siblings, Arch. Int. Med. 80: 249 (Aug.) 1947.
- 1699. Robinson, W. D.: Nutrition and arthritis, Nutrition Rev. 7: 33 (Feb.) 1949.
- 1700. Robinson, W. D.: Present status of ACTH and cortisone in the practical management of rheumatoid arthritis, J. Michigan M. Soc. 49: 1045 (Sept.) 1950.
- 1701. Robinson, W. D., and Block, W. D.: Protein metabolism in rheumatoid arthritis, Proc. Central Soc. Clin. Research 20: 90, 1947; also J. Lab. and Clin. Med. 32: 1551 (Dec.) 1947.
- 1702. Robinson, W. D., Conn, J. W., Block, W. D., Louis, L. H., and Katz, J.: Role of the anterior pituitary and adrenal cortex in urate metabolism and gout, 7th Inter. Congress Rheumatic Diseases: Abst. Ann. Rheumat. Dis. 8: 312 (Dec.) 1949.
- 1703. Robles, G. J.: Incidence and clinical features of rheumatic fever in Mexico City, Am. Heart J. 33: 713 (May) 1947.
- 1704. Robson, H. N.: Observations on capillary function, 1950 Proc. Int. Soc. Hematology, 1950, Grune & Stratton, New York, p. 537.
- 1705. Robson, H. N., and Duthie, J. J. R.: Capillary resistance and adrenocortical activity, Brit. M. J. 2: 971 (Oct.) 1950.
- 1706. Rockwell, G. E.: The role of allergy in rheumatoid arthritis and a suggested treatment; preliminary report, Ann. Allergy 7: 195 (Mar.-Apr.) 1949.
- 1707. Rogen, A. S.: Heart in rheumatoid arthritis, Brit. M. J. 1: 87 (Jan.) 1947.
- 1708. Rogers, H. M., and Langley, F. H.: Neutropenia associated with splenomegaly and atrophic arthritis (Felty's syndrome); report of a case in which splenectomy was performed, Ann. Int. Med. 32: 745 (Apr.) 1950.
- 1709. Rogers, L.: Upper-limb pain due to lesions of thoracic outlet. The scalenus syndrome, cervical rib and costoclavicular compression, Brit. M. J. 2: 956 (Oct.) 1949.
- 1710. Rogoff, B., and Freyberg, R. H.: The familial incidence of rheumatoid spondylitis, Ann. Rheumat. Dis. 8: 139 (June) 1949.
- 1711. Rogoff, B., Freyberg, R. H., Powell, H. M., and Rice, R. M.: Experiences with antireticular cytotoxic serum (ACS) in arthritis, Am. J. M. Sc. 214: 395 (Oct.) 1947.
- 1712. Romer, C.: Treatment of abortus fever with sulfonamides and blood transfusion, Brit. M. J. 1: 1035 (June) 1949.
- 1713. Ronchese, F.: Dermofragility with dermo-hyperlaxity-hyperelasticity and arthro-hyper-laxity (Ehlers-Danlos syndrome); additional data on a case reported 12 years previously, Rhode Island M. J. 32: 80 (Feb.) 1949.
- 1714. Ropes, M. W., Kaufman, D., and Perlmann, G. E.: Variations in the electrophoretic pattern of synovial fluid in articular disease, J. Clin. Investigation 28: 807, 1949.
- 1715. Ropes, M. W., Robertson, W. B., Rossmeisl, E. C., Peabody, R. B., and Bauer, W.: Synovial fluid mucin, Acta med. Scandinav., supp. 196: 700, 1947.
- 1716. Rose, M. H., Littmann, D., and Houghton, J.: Polyarteritis nodosa: clinical and pathological study and report of 6 cases, Ann. Int. Med. 32: 1114 (June) 1950.
- 1717. Rose, H. M., Ragan, C., Pearce, E., and Lipman, M. O.: Differential agglutination of normal and sensitized sheep erythrocytes by sera of patients with rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 68: 1 (May) 1948.
- 1718. Rose, P. A.: Treatment of rheumatoid arthritis; results with new gold compound of low toxicity, Illinois M. J. 92: 175 (Sept.) 1947.
- 1719. Rose, T. F.: Bilateral trigger thumb in infants, M. J. Australia 1: 18 (Jan.) 1946.
- 1720. Rosellini, L. J., and van Rooy, C. W.: Delayed allergic reaction to penicillin in oil and wax treated with procaine, intravenously, Northwest Med. 45: 849 (Nov.) 1946.
- 1721. Rosenberg, C., and Schloss, B.: Plasma hexosamine levels in acute rheumatic fever, Am. Heart J. 38: 872 (Dec.) 1949.

- 1722. Rosenberg, D. H.: Symposium on advances in clinical medicine; rheumatic fever in adult, M. Clin. North America 31: 94 (Jan.) 1947.
- 1723. Rosenberg, E. F.: Diamidines in chemotherapy; survey of recent developments with note regarding therapeutic trials in patients with rheumatoid arthritis, Ann. Int. Med. 25: 832 (Nov.) 1946.
- 1724. Rosenberg, E. F.: Arthritis. Comments on differential diagnosis and new developments in therapy, J. A. M. A. 140: 759 (July) 1949.
- 1725. Rosenberg, E. F.: Rheumatoid arthritis, with especial reference to its treatment, Veterans Administration Technical Bulletin TB 10-60: 1, Dec. 1949.
- 1726. Rosenberg, E. F., and Arens, R. A.: Gout; clinical, pathologic and roentgenographic observations, Radiology 49: 169 (Aug.) 1947.
- 1727. Rosenberg, E. F., Bishop, L. F., Jr., Weintraub, H. J., and Hench, P. S.: Cardiac lesions in rheumatoid arthritis; a summary of recent developments and a bedside study of patients and controls, Arch. Int. Med. 85: 751 (May) 1950.
- 1728. Rosenberg, E. F., and Hench, P. S.: Recent advances in treatment of rheumatic fever, with special reference to sulfonamide prophylaxis and intravenous salicylate therapy, M. Clin. North America 30: 489 (May) 1946.
- 1729. Rosenblatt, W. H.: Rheumatic fever; clinical survey of 542 cases, with reference to unusual precipitating factors, case reports, Kentucky M. J. 44: 222 (July) 1946.
- 1730. Rosenblum, H.: Rheumatic fever control program in California, California Med. 66: 233 (Apr.) 1947.
- 1731. Rosenblum, H., and Fraser, L. E.: Effect of para-aminobenzoic acid on fever and joint pains of acute rheumatic fever, Proc. Soc. Exper. Biol. and Med. 65: 178 (June) 1947.
- 1732. Rosenthal, I. H.: Generalized scleroderma (hidebound disease, its relation to oral cavity, with case history and dental restoration), Oral Surg., Oral Med. and Oral Path. 1: 1019 (Nov.) 1948.
- 1733. Rosenthal, S. R.: Pathological and experimental studies of Boeck's sarcoid. Report of a case with panarteritis, periarteritis, terminal-hypertension and uremia, and the reproduction of a sarcoid-like lesion in guinea pigs, Am. Rev. Tuberc. 60: 236 (Aug.) 1040
- 1734. Ross, D. N.: Oral and intravenous iron therapy in the anaemia of rheumatoid arthritis, Ann. Rheumat. Dis. 9: 358 (Dec.) 1950.
- 1735. Ross, P. J.: Incidence of abnormal oronasal lymphoid tissue in rheumatic fever patients, M. Clin. North America 30: 540 (May) 1946.
- 1736. Rothbard, S., Watson, R. F., Swift, H. F., and Wilson, A. T.: Bacteriologic and immunologic studies on patients with hemolytic streptococcic infections as related to rheumatic fever, Arch. Int. Med. 82: 229 (Sept.) 1948.
- 1737. Rothman, S., and Felsher, Z.: Symposium on advances in clinical medicine; subacute and acute disseminated lupus erythematodes, M. Clin. North America 31: 198 (Jan.) 1947.
- 1738. Rothman, S., and Walker, S.: Scleroderma, M. Clin. North America 33: 55 (Jan.) 1949.
- 1739. Rothschild, C. E.: Aseptic necrosis of femoral head simulating tuberculosis, Bull. Hosp. Joint Dis. 10: 226 (Oct.) 1949.
- 1740. Routh, J. I., and Paul, W. D.: Electrophoretic analyses of plasma and serum proteins in rheumatoid arthritis, Arch. Phys. Med. 31: 511 (Aug.) 1950.
- 1741. Rubbo, S. D., Holmes, M. C., and Stokes, H. L.: Prophylactic sulphanilamide in rheumatic fever; review of 548 cases, Lancet 2: 311 (Aug.) 1949.
- 1742. Russell, G. R.: Brucellosis in children, J. Oklahoma M. A. 40: 82 (Mar.) 1947.
- 1743. Russell, D. A., and Smith, C. D.: Pellegrini-Stieda disease, Radiology 46: 351 (Apr.) 1946.
- 1744. Russell, L. W.: Hip disorders in children; differential diagnosis, Illinois M. J. 97: 273 (May) 1950.

- 1745. Rutstein, D. D.; Rheumatic fever community program; its value in epidemiologic study of rheumatic fever; summary of symposium, Am. J. Pub. Health 38: 1082 (Aug.) 1948.
- 1746. Ryan, C. A.: Tuberculosis of bones and joints, J. Internat. Coll. Surgeons 12: 36 (Jan.-Feb.) 1949.
- 1747. Rytand, D. A., Burnham, DeW. K., and Cox, A. J.: Periarteritis nodosa following the dermatitis of poison oak and of primrose, Stanford M. Bull. 6: 319 (May) 1948.
- 1748. Sacassa, C. F.: The diagnosis and treatment of gout, Ann. West. Med. and Surg. 2: 307 (July) 1948.
- 1749. Sacks, D. R., Inmon, T. W., and O'Neill, J. R.: Diffuse scleroderma, Texas State J. Med. 46: 37 (Jan.) 1950.
- 1750. Saenger, E. L.: Unilateral paraspinal abscess, Radiology 48: 256 (Mar.) 1947.
- 1751. Salassa, R. M., Bollman, J. L., and Dry, T. J.: The effect of para-aminobenzoic acid on the metabolism and excretion of salicylate, J. Lab. and Clin. Med. 33: 1393 (Nov.) 1948.
- 1752. Salem, E. P.: Low back pain due to narrowing of intervertebral foramen, Bull. Hosp. Joint Dis. 8: 187 (Oct.) 1947.
- 1753. Salomon, M. I.: Palindromic rheumatism in children, New York State J. Med. 46: 622 (Mar.) 1946.
- 1754. Samuel, E. P.: The innervation of the articular capsule of the knee joint, J. Anat. 83: 80 (Jan.) 1949.
- Sandler, B. P., Matthews, J. H., and Bornstein, S.: Pulmonary cavitation due to polyarteritis, J. A. M. A. 144: 754 (Oct.) 1950.
- 1756. Sandweiss, D. J., Saltzstein, H. C., Scheinberg, S. R., and Parks, A.: Hormone studies in peptic ulcer; pituitary adrenocorticotropic hormone (ACTH) and cortisone, J. A. M. A. 144: 1436 (Dec.) 1950.
- 1757. Sargent, J. C.: Reiter's syndrome, J. Urol. 54: 556 (Dec.) 1945.
- 1758. Sashin, D.: Coccidioidomycosis with involvement of bone, Bull. Hosp. Joint Dis. 8: 59 (Apr.) 1947.
- 1759. Saslaw, M. S., Ross, B. D., and Dobrin, M.: The incidence of rheumatic heart disease in native school children of Dade County, Florida, Am. Heart J. 40: 760 (Nov.) 1950.
- 1760. Saunders, R. L. de C. H., and Young, E. G.: Absorption of trypan blue from human knee joint, J. Bone and Joint Surg. 29: 301 (Apr.) 1947.
- 1761. Savage, O.: Speransky's method of spinal pumping in rheumatoid arthritis; a review of 4 cases, Brit. M. J. 1: 496 (Mar.) 1948.
- 1762. Savage, O.: Frozen shoulder, M. Press 221: 623 (June) 1949.
- 1763. Savage, O.: Cortisone (compound E) and adrenocorticotropic hormone in rheumatoid arthritis, Proc. Roy. Soc. Med. 43: 11 (Jan.) 1950.
- 1764. Sawicky, H. H.: Therapy of lupus crythematosus; bismuth sodium triglycollamate, sodium para-aminobenzoate and the tocopherols (vitamin E), Arch. Dermat. and Syph. 61: 906 (June) 1950.
- 1765. Sayers, G.: The adrenal cortex and homeostasis, Physiol. Rev. 30: 241 (July) 1950.
- 1766. Sayers, G., Burns, T. W., Tyler, F. H., and Jager, B. V.: Metabolic actions and fate of intravenously administered adrenocorticotropic hormone in man, J. Clin. Endocrinol. 9: 593 (July) 1949.
- 1767. Scadding, J. G.: Acute benign dry pleurisy in the Middle East, Lancet 1: 763 (May) 1946.
- 1768. Schaefer, L. E., Rashkoff, I. A., and Megibow, R. S.: Sodium gentisate in the treatment of acute rheumatic fever, Circulation 2: 265 (Aug.) 1950.
- 1769. Schapiro, S.: Low back and rectal pain from an orthopedic and proctologic viewpoint with review of 180 cases, Am. J. Surg. 79: 117 (Jan.) 1950.
- 1770. Schatzki, R.: Roentgenologic appearance of the gastrointestinal tract in scleroderma, Bull. New England M. Center 8: 211, 1946.

- 1771. Scheele, L. A.: Arthritis as a public health problem, Pub. Health Rep. 65: 1351 (Oct.) 1950.
- 1772. Scheie, H. G., Crandall, A. S., and Henle, W.: Keratitis associated with lymphogranuloma venereum, J. A. M. A. 135: 333 (Oct.) 1947.
- 1773. Scheinberg, D.: Unique heart tetralogy with palindromic rheumatism, J. Tennessee M. A. 40: 260 (Aug.) 1947.
- 1774. Schirmer, R. E.: Increased capillary fragility following use of cortone acetate in treatment of arthritis, J. Arkansas M. Soc. 47: 99 (Nov.) 1950.
- 1775. Schlesinger, B.: Arthritis in young, Brit. M. J. 2: 197 (July) 1949.
- 1776. Schlesinger, E. B., and Ragan, C.: "Muscle spasm" in acute low back pain and similar syndromes; new method of treatment with curare (d-tubocurarine in oil and wax), Am. J. Med. 1: 621 (Dec.) 1946.
- 1777. Schmidt, L.: Physiotherapy in rheumatic diseases; choice of suitable methods at various stages, Brit. J. Phys. Med. 9: 104 (July-Aug.) 1946.
- 1778. Schmith, K., and Faber, V.: The turbidimetric method for determination of hyaluronidase, Scandinav. J. Clin. and Lab. Invest. 2: 292, 1950.
- 1779. Schmitt, F. O., and Gross, J.: Further progress in the electron microscopy of collagen, J. Am. Leather Chem. Assoc. 43: 658 (Nov.) 1948.
- 1780. Schneider, R. W., and Kammer, H.: Hypervitaminosis D. Report of 9 cases, Cleve-land Clin. Quart. 15: 82 (Apr.) 1948.
- 1781. Schultz, M. P.: Rheumatic fever; current considerations, M. Ann. District of Columbia 16: 243 (May) 1947.
- 1782. Schultz, M. P., and Rose, E. J.: "Albumin-bacterioplasma conjugates" with special reference to the etiology of rheumatic fever; preliminary report, Pub. Health Rep. 62: 1009 (July) 1947.
- 1783. Schwarz, G. S., and Skinsnes, O. K.: Generalized progressive scleroderma; report of an instance of esophagoscopic perforation of the esophagus with description of the roentgenological and necropsy findings, Am. J. Roentgenol. 62: 359 (Sept.) 1949.
- 1784. Schwartz, S., and Steinbrocker, O.: Production of rheumatic subcutaneous nodules, Am. Heart J. 40: 100 (July) 1950.
- 1785. Schwartz, T. B., and Engel, F. L.: Effect of adrenocorticotropic hormone and cortisone therapy on human plasma aminopeptidase activity, Proc. Soc. Exper. Biol. and Med. 74: 82 (May) 1950.
- 1786. Schwartzman, J.: Chorea minor; review of 175 cases with reference to etiology, treatment and sequelae, Rheumatism 6: 89 (Apr.) 1950.
- 1787. Schwartzman, J., McDonald, D. H., and Perillo, L.: Sydenham's chorea; report of 140 cases and review of the recent literature, Arch. Pediat. 65: 6 (Jan.) 1948.
- 1788. Scott, G. L.: Practical note on rheumatic fibrositis, M. Press 220: 391 (Nov.) 1948.
- 1789. Scott, J. W.: Brucellosis, Canad. M. A. J. 56: 414 (Apr.) 1947.
- 1790. Scott, R. A. M.: Allergic reactions to penicillin, Brit. M. J. 1: 110 (Jan.) 1947.
- 1791. Scott, W.: Pain in shoulder and arm, Ann. West. Med. and Surg. 2: 522 (Nov.) 1948.
- 1792. Scoville, W. B., Moretz, W. H., and Hankins, W. D.: Discrepancies in myelography; statistical survey of 200 operative cases undergoing pantopaque myelography, Surg., Gynec. and Obst. 86: 559 (May) 1948.
- 1793. Scuderi, C.: Backache from an industrial standpoint, S. Clin. North America 29: 215 (Feb.) 1949.
- 1794. Scully, F. J.: Vitamin therapy in arthritis, M. Times, New York 76: 281 (July) 1948.
- 1795. Seddon, H. J., and Alexander, G. L.: Discussion on spinal caries with paraplegia, Proc. Roy. Soc. Med. 39: 723 (Sept.) 1946.
- 1796. Sedgwick, R. P., and Von Hagen, K. O.: Neurological manifestations of lupus erythematosus and periarteritis nodosa; report of 10 cases, Bull. Los Angeles Neurol. Soc. 13: 129 (Sept.) 1948.

1797. Seidenstein, H.: Acute pain in the wrist and hand associated with calcific deposits; report of 15 cases, J. Bone and Joint Surg. 32A: 413 (Apr.) 1950.

1798. Seifter, J., Baeder, D. H., and Dervinis, A.: Alteration in permeability of some membranes by hyaluronidase and inhibition of this effect by steroids, Proc. Soc. Exper. Biol. and Med. 72: 136 (Oct.) 1949.

1799. Seifter, J., Baeder, D. H., and Begany, A. J.: Influence of hyaluronidase and steroids on permeability of synovial membrane, Proc. Soc. Exper. Biol. and Med. 72: 277 (Nov.) 1949.

1800. Seifter, J., Ehrich, W. E., Begany, A. J., and Warren, G. H.: Effects of cortisone, hyaluronidase, desoxycorticosterone, and artisone on experimental serum disease in rabbits, Proc. Soc. Exper. Biol. and Med. 75: 337, 1950.

1801. Seifter, J., Warter, P. J., and Fitch, D. R.: Preliminary observations on the antiarthritic effect of 21-acetoxypregnenolone, Proc. Soc. Exper. Biol. and Med. 73: 131 (Jan.) 1950.

1802. Seldin, D. W., Kaplan, H. S., and Bunting, H.: Rheumatic pneumonia, Ann. Int. Med. 26: 496 (Apr.) 1947.

1803. Seligson, F.: Poncet's disease; clinical observations on inflammatory and degenerative joint reactions in tuberculosis, Am. Rev. Tuberc. 52: 463 (Dec.) 1945.

1804. Selye, H.: General adaptation syndrome and the diseases of adaptation, J. Clin. Endocrinol. 6: 117 (Feb.) 1946.

1805. Selye, H.: The alarm reaction and the diseases of adaptation, Ann. Int. Med. 29: 403 (Sept.) 1948.

1806. Selye, H.: Further studies concerning the participation of the adrenal cortex in the pathogenesis of arthritis, Brit. M. J. 2: 1129 (Nov.) 1949.

1807. Selye, H.: Stress and the general adaptation syndrome (Heberden oration), Brit. M. J. 1: 1383 (June) 1950.

1808. Selye, H., and Stone, H.: Influence of diet upon nephrosclerosis, periarteritis nodosa and cardiac lesions produced by "endocrine kidney," Endocrinology 43: 21 (July) 1948.

1809. Selye, H., and Stone, H.: Pathogenesis of the cardiovascular and renal changes which usually accompany malignant hypertension, J. Urol. 56: 399 (Oct.) 1946.

1810. Semmes, R. E.: Lateral rupture of cervical intervertebral discs; incidence and clinical varieties, Am. J. Surg. 75: 137 (Jan.) 1948.

1811. Senturia, H. R., and Simon, H. E.: Traumatic lipohemarthrosis; layering of fat and blood in a joint, Am. J. Surg. 73: 79 (Jan.) 1947.

1812. Seth-Smith, D. W.: Radiological interpretation of chronic rheumatic arthritis, Rheumatism 4: 186 (Apr.) 1948.

1813. Shaffer, J. M., and Spink, W. W.: Therapy of experimental brucella infection in the developing chick embryo; infection and therapy via yolk sac, J. Immunol. 59: 393 (Aug.) 1948.

1814. Shaffer, M. F., and Rake, G.: Studies on lymphogranuloma venereum; evaluation of the complement fixation test with lygranum, J. Lab. and Clin. Med. 32: 1060 (Sept.) 1947.

1815. Shapiro, E., Lipkis, M. L., Kahn, J., and Heid, J. B.: Electrocardiographic changes in acute gonococcal arthritis and myocarditis simulating acute rheumatic polyarthritis, Am. J. M. Sc. 217: 300 (Mar.) 1949.

1816. Shaw, R. S.: Ruptured intervertebral disk from positive acceleration, J. Aviation Med. 19: 276 (Aug.) 1948.

1817. Sheldon, W.: Tuberculous rheumatism, Lancet 1: 119 (Jan.) 1946.

1818. Shemin, D., and Rittenberg, D.: On the utilization of glycine for uric acid synthesis in man, J. Biol. Chem. 167: 875 (Mar.) 1947.

1819. Sheppard, C. W., Wells, E. B., Hahn, P. F., and Goodell, J. P. B.: Studies of distribution of intravenously administered colloidal sols of manganese dioxide and gold in

- human beings and dogs using radioactive isotopes, J. Lab. and Clin. Med. 32: 274 (Mar.) 1947.
- 1820. Sherwood, K. K., and Zimmerman, B.: Office management of chronic arthritis, Northwest Med. 46: 30 (Jan.) 1947.
- 1821. Sherwood, K. K., and Zimmerman, B.: Fibrositis and psychogenic backache, Northwest Med. 48: 465 (July) 1949.
- 1822. Shetlar, M. R., Foster, J. V., Kelly, K. H., and Everett, M. R.: Serum polysaccharide level in the normal state, Proc. Soc. Exper. Biol. and Med. 69: 507 (Dec.) 1948.
- 1823. Shetlar, M. R., Shetlar, C. L., Richmond, V., and Everett, M. R.: Polysaccharide content of serum fractions in carcinoma, arthritis, and infections, Cancer Research 10: 681 (Nov.) 1950.
- 1824. Shick, R. M., Baggenstoss, A. H., Fuller, B. F., and Polley, H. F.: Effects of cortisone and ACTH on periarteritis nodosa and cranial arteritis, Proc. Staff Meet., Mayo Clin. 25: 492 (Aug.) 1950.
- 1825. Shields, C. D., and Smith, E. M.: Keratosis blennorrhagica treated with penicillin and hyperpyrexia, South. M. J. 42: 623 (July) 1949.
- 1826. Shipp, F. L., and Haggart, G. E.: Further experience in the management of osteitis condensans ilii, J. Bone and Joint Surg. 32A: 841 (Oct.) 1950.
- 1827. Short, C. L.: Arthritis in Mediterranean Theater of Operations; incidence of joint disease—clinical description of rheumatoid arthritis, New England J. Med. 236: 383 (Mar.) 1947.
- 1828. Short, C. L.: Arthritis in Mediterranean Theater of Operations; clinical description of hypertrophic arthritis, arthralgia and psychogenic rheumatism, New England J. Med. 236: 429 (Mar.) 1947.
- 1829. Short, C. L.: Arthritis in Mediterranean Theater of Operations; clinical description of infectious and other types of arthritis. New England J. Med. 236: 468 (Mar.) 1947.
- 1830. Short, C. L., Abrams, N. R., and Sartwell, P. E.: Factors associated with the onset of rheumatoid arthritis; a statistical study of 293 patients and controls, Ann. Rheumat. Dis. 8: 313, 1949.
- 1831. Short, C. L., Beckman, W. W., and Bauer, W.: Medical progress; gold therapy in rheumatoid arthritis, New England J. Med. 235: 362 (Sept.) 1946.
- 1832. Short, C. L., and Bauer, W.: The course of rheumatoid arthritis in patients receiving simple medical and orthopedic measures, New England J. Med. 238: 142 (Jan.) 1948.
- 1833. Short, D. S.: Case of rheumatoid arthritis simulating pyogenic infection, Brit. M. J. 2: 204 (July) 1949.
- 1834. Shorvon, L. M.: Gout in leukaemia; report of case, Lancet 2: 378 (Sept.) 1946.
- 1835. Shulman, B., and Cohen, D.: Dermatomyositis, Illinois M. J. 97: 102 (Feb.) 1950.
- 1836. Shulman, J.: Bismuth therapy and physiotherapy in rheumatoid arthritis, Brit. J. Phys. Med. 10: 8 (Jan.-Feb.) 1947.
- 1837. Shuman, C. R., and Finestone, A. J.: Inhibition of hyaluronidase in vitro by adrenal cortical activation, Proc. Soc. Exper. Biol. and Med. 73: 248, 1950.
- 1838. Shwartzman, G., Schneierson, S. S., and Soffer, L. J.: Suppression of the phenomenon of local tissue reactivity by ACTH, cortisone, and sodium salicylate, Proc. Soc. Exper. Biol. and Med. 75: 175 (Oct.) 1950.
- 1839. Sideman, S., Glassman, F., and Wolin, I.: Chondromalacia patellae, S. Clin. North America 29: 261 (Feb.) 1949.
- 1840. Sieracki, L. A.: Post-convalescent care of rheumatic fever, Rhode Island M. J. 28: 720 (Oct.) 1945.
- 1841. Silberberg, M., and Silberberg, R.: Effects of high fat diet on joints of aging mice, Arch. Path. 50: 828 (Dec.) 1950.
- 1842. Silberberg, M., and Silberberg, R.: Some aspects of role of hormonal and nutritional factors in skeletal growth and development, Growth 13: 359 (Dec.) 1949.

- 1843. Silberberg, R., and Silberberg, M.: Skeletal growth and articular changes in mice receiving high-fat diet, Am. J. Path. 26: 113 (Jan.) 1950.
- 1844. Silberberg, R., and Silberberg, M.: Growth and articular changes in slowly and rapidly developing mice fed a high-fat diet, Growth 14: 213 (Sept.) 1950.
- 1845. Silverman, H., and Gubernick, I.: Colorimetric determination of uric acid with alkaline ferricyanide, J. Biol. Chem. 167: 363 (Feb.) 1947.
- 1846. Simmonds, F. A.: Shoulder pain, with particular reference to "frozen" shoulder, J. Bone and Joint Surg. 31B: 426 (Aug.) 1949.
- 1847. Simonsen, M.: On the effect of cortisone on allergy and complement titer, Scandinav. J. Clin. and Lab. Invest. 2: 287, 1950.
- 1848. Simpson, N. R. W.: Treatment of ankylosing spondylitis, Rheumatism 6: 53 (Apr.) 1950.
- 1849. Simpson, N. R. W., and Brooks, D. H.: Effect of blood transfusion on rheumatoid arthritis, Proc. Roy. Soc. Med. 41: 609 (Sept.) 1948.
- 1850. Simpson, N. R. W., Kersley, G. D., and Brooks, D. H.: Effect of blood transfusion on rheumatoid arthritis, Ann. Rheumat. Dis. 8: 277 (Dec.) 1949.
- 1851. Simpson, N. R. W., and Stevenson, C. J.: An analysis of 200 cases of ankylosing spondylitis, Brit. M. J. 1: 214 (Feb.) 1949.
- 1852. Simpson, T. R.: Case of osteochondritis dissecans of ankles, Brit. J. Surg. 37: 359 (Jan.) 1950.
- 1853. Sinclair, R. J. G., and Duthie, J. J. R.: Salazopyrin in treatment of rheumatoid arthritis, Ann. Rheumat. Dis. 8: 226 (Sept.) 1949.
- 1854. Sinclair, R. J. G., and Duthie, J. J. R.: Intravenous iron in hypochromic anemia associated with arthritis, Lancet 2: 646 (Oct.) 1949.
- 1855. Sinclair, R. J. G., and Duthie, J. J. R.: Intravenous iron in treatment of hypochromic anemia associated with rheumatoid arthritis, Brit. M. J. 2: 1257 (Dec.) 1950.
- 1856. Skouby, A. P.: Scleroderma-like picture following a single serum injection, Acta med. Scandinav. 136: 51, 1949.
- 1857. Skouby, A. P., and Teilum, G.: Progressive systemic sclerosis with dominating gastrointestinal disturbances, Acta med. Scandinav. 137: 111, 1950.
- 1858. Small, J. C.: The mechanics of deformities of the hands in atrophic arthritis and a discussion of their prevention and correction, Ann. Int. Med. 32: 1087 (June) 1950.
- 1859. Smith, A. D.: Tuberculosis of bones and joints, Arch. Surg. 58: 546 (Apr.) 1949.
- 1860. Smith, A. D.: Some causes of low back pain, Tr. A. Life Insur. M. Dir. America (1949) 33: 23, 1950.
- 1861. Smith, A. DeF., and Yu, H. I.: Streptomycin combined with surgery in the treatment of bone and joint tuberculosis, J. A. M. A. 142: 1 (Jan.) 1950.
- 1862. Smith, C. C., and Zeek, P. M.: Studies on periarteritis nodosa; role of various factors in etiology of periarteritis nodosa in experimental animals, Am. J. Path. 23: 147 (Jan.) 1947.
- 1863. Smith, C. E., Beard, R. R., Rosenberger, H. G., and Whiting, E. G.: Effect of season and dust control on coccidioidomycosis, J. A. M. A. 132: 833 (Dec.) 1946.
- 1864. Smith, C. E., Beard, R. R., Whiting, E. G., and Rosenberger, H. G.: Varieties of coccidioidal infection in relation to epidemiology and the control of diseases, Am. J. Pub. Health 36: 1394 (Dec.) 1946.
- 1865. Smith, F. B.: Vitallium cup arthroplasty in the treatment of degenerative arthritis of the hip: report of 6 cases, Portland Clin. Bull. 3: 29 (Sept.) 1949.
- 1866. Smith, F. H.: Charcot-like joints in yaws, U. S. Nav. M. Bull. 46: 1832 (Dec.) 1946.
- Smith, L. DeS., and George, R. L.: Anaerobic bacterial flora of clostridial myositis, J. Bact. 51: 271 (Mar.) 1946.
- 1868. Smith, P. K., Gleason, H. L., Stoll, C. G., and Ogorzalek, S.: Studies on the pharmacology of salicylates, J. Pharmacol. and Exper. Therap. 87: 237 (July) 1946.

- 1869. Smith-Peterson, M. N.: Evolution of mould arthroplasty of the hip joint, J. Bone and Joint Surg. 30B: 59 (Feb.) 1948.
- 1870. Smith, R. T.: Treatment of rheumatoid arthritis and other rheumatic conditions with salicylate and para-aminobenzoic acid; a study of 125 patients, Journal Lancet 70: 192 (May) 1950.
- 1871. Smith, R. W., Margulis, R. R., Brennan, M. J., and Monto, R. W.: The influence of ACTH and cortisone on certain factors of blood coagulation, Science 112: 295 (Sept.) 1950.
- 1872. Smith, S., and McCabe, E. S.: Primary splenic neutropenia with arthritis (so-called Felty syndrome); its treatment by splenectomy, Ann. Int. Med. 29: 445 (Sept.) 1948.
- 1873. Smull, K., Wissler, R. W., and Watson, J. M.: The effect of sodium salicylate upon serum disease in rabbits, J. Lab. and Clin. Med. 33: 936 (Aug.) 1948.
- 1874. Smyth, C. J., Cotterman, C. W., and Freyberg, R. H.: The genetics of gout and hyper-uricemia—an analysis of 19 families, J. Clin. Investigation 27: 749 (Nov.) 1948.
- 1875. Smyth, C. J., Stecher, R. M., and Wolfson, W. Q.: Genetic and endocrine determinants of the plasma urate level, Science 108: 514 (Nov.) 1948.
- 1876. Snively, G. G., and Glick, D.: Mucolytic enzyme systems; serum hyaluronidase inhibitor in liver disease, J. Clin. Investigation 29: 1087 (Aug.) 1950.
- 1877. Snorrason, E.: Articular pain in scarlet fever, Acta med. Scandinav. 124: 67, 1946.
- 1878. Snyder, C. H.: Sling for use in Legg-Perthes disease, J. Bone and Joint Surg. 29: 524 (Apr.) 1947.
- 1879. Soeur, R.: The synovial membrane of the knee in pathological conditions, J. Bone and Joint Surg. 31A: 317 (Apr.) 1949.
- 1880. Soffer, L. J., Levitt, M. F., and Baehr, G.: Use of cortisone and adrenocorticotropic hormone in acute disseminated lupus erythematosus, Arch. Int. Med. 86: 558 (Oct.) 1950.
- 1881. Sokoloff, L., Wilens, S. L., Bunim, J. J., and McEwen, C.: Diagnostic value of histologic lesions of striated muscle in rheumatoid arthritis, Am. J. M. Sc. 219: 174 (Feb.) 1950.
- 1882. Sokolow, M.: Significance of electrocardiographic changes in rheumatic fever, Am. J. Med. 5: 365 (Sept.) 1948.
- 1883. Sokolow, M., and Snell, A. M.: Atypical features of rheumatic fever in young adults, J. A. M. A. 133: 981 (Apr.) 1947.
- 1884. Solomon, A. P.: Low back pain; the psychosomatic viewpoint—a psychosomatic study on increased muscle tension of the voluntary musculature as a factor in the production of low back pain and in the pathogenesis of atrophic and hypertrophic arthritis of the spine—a preliminary report, Indust. Med. 18: 6 (Jan.) 1949.
- 1885, Solomon, W. M.: Physical treatment of arthritis, J. A. M. A. 136: 128 (May) 1948.
- 1886. Solomon, W. M., and Stecher, R. M.: Chronic absorptive arthritis or opera-glass hand report of 8 cases, Ann. Rheumat. Dis. 9: 209 (Sept.) 1950.
- 1887. Solovay, J., and Solovay, H. U.: Paraplegic neuroarthropathy, Am. J. Roentgenol. 61: 475 (Apr.) 1949.
- 1888. Sommerville, I. F., Marrian, G. F., Duthie, J. J. R., and Sinclair, R. J. G.: Abnormality in steroid metabolism associated with rheumatoid arthritis, Lancet 1: 116 (Jan.) 1950.
- 1889. Sonne, J. C., Buchanan, J. M., and Delluva, A. M.: Biological precursors of uric acid; role of lactate, acetate, and formate in synthesis of ureide groups of uric acid, J. Biol. Chem. 173: 69 (Mar.) 1948.
- 1890. Sorrel, E., and Sorrel-Dejerine, Mme.: Immobilization with bone grafts in the treatment of tuberculosis of joints and Pott's disease, J. Bone and Joint Surg. 29: 603 (July) 1947.
- 1891. Sorsby, A., and Gormaz, A.: Iritis in rheumatic affections, Brit. M. J. 1: 597 (Apr.)

1892. Spain, D. M., and Thomas, A. G.: The pulmonary manifestations of scleroderma; an anatomic-physiological correlation, Ann. Int. Med. 32: 152 (Jan.) 1950.

1893. Spencer, G. N.: Experience with gout at Wood Hospital, Marquette M. Rev. 14: 57 (Jan.) 1949.

1894. Sperling, I. L.: Tendon sheath involvement in rheumatic diseases, J. M. Soc. New Jersey 46: 430 (Sept.) 1949.

Sperling, I. L.: Rheumatic polytendovaginitis, Ann. Rheumat. Dis. 9: 43 (Mar.) 1950.
 Spies, T. D., and Stone, R. E.: Relief of the symptoms of acute gout and rheumatoid arthritis by means of pituitary adrenocorticotropic hormone (ACTH), South. M. J.

42: 720 (Aug.) 1949.

1897. Spies, T. D., Stone, R. E., deMaeyer, E., and Niedermeier, W.: Deoxycortone with ascorbic acid versus adrenocorticotropic hormone in rheumatoid arthritis, Lancet 2: 1219 (Dec.) 1949.

1898. Spink, W. W.: Pathogenesis of human brucellosis with respect to prevention and treatment, Ann. Int. Med. 29: 238 (Aug.) 1948.

1899. Spink, W. W., Braude, A. I., Çastaneda, M. R., and Goytia, R. S.: Aureomycin therapy in human brucellosis due to *Brucella melitensis*, J. A. M. A. 138: 1145 (Dec.) 1948.

1900. Spink, W. W., Hall, W. H., Shaffer, J. M., and Braude, A. I.: Brucellosis: specific therapy in patients having bacteremia, Tr. Am. Clin. and Climatol. A. (1947) 59: 19, 1948.

 Spishakoff, N. M., and Low-Beer, B. V. A.: Roentgen therapy of rheumatoid spondylitis, California Med. 70: 124 (Feb.) 1949.

1902. Spitz, H., Steinbrocker, O., Schwartz, S., and Schittone, M.: Fulminating fatal gout, Am. J. Med. 6: 513 (Apr.) 1949.

1903. Spitzer, N., and Steinbrocker, O.: The treatment of gonorrheal arthritis with penicillin, Am. J. M. Sc. 218: 138 (Aug.) 1949.

1904. Splithoff, C. A.: Chronic lumbar backache, Am. J. Surg. 71: 19 (Jan.) 1946.

1905. Sprague, R. G., Power, M. H., and Mason, H. L.: Physiological effects of cortisone and pituitary adrenocorticotropic hormone (ACTH) in man, J. A. M. A. 144: 1341 (Dec.) 1950.

1906. Sprague, R. G., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: Observations on the physiologic effects of cortisone and ACTH in man, Arch. Int. Med. 85: 199 (Feb.) 1950.

1907. Spray, P. E., and Ghormley, R. K.: Histories and physical findings in 50 cases of chondromalacia, Proc. Staff Meet., Mayo Clin. 25: 527 (Aug.) 1950.

1908. Sprecher, E. E.: Trigger thumb in infants, J. Bone and Joint Surg. 31A: 672 (July) 1949.

 Sprecher, M. H., and Copeland, J. R.: Haverhill fever due to Streptobacillus moniliformis treated with streptomycin, J. A. M. A. 134: 1014 (July) 1947.

1910. Sprechler, M.: Investigations on the urinary excretion of corticoids and 17-ketosteroids during the administration of adrenocorticotrophic hormone (ACTH), Acta endocrinol. 5: 101, 1950.

1911. Sprinz, H.: A case of synovial sarcoma with metastases, Bull. U. S. Army M. Dept. 9: 131 (Feb.) 1949.

1912. Spurling, R. G., and Grantham, E. G.: Ruptured intervertebral discs in lower lumbar regions, Am. J. Surg. 75: 140 (Jan.) 1948.

1913. Stack, J. K.: Acute and chronic bursitis in the region of the elbow joint, S. Clin. North America 29: 155 (Feb.) 1949.

1914. Stack, J. K.: The injured knee; the negative x-ray, Indust. Med. 18: 91 (Mar.) 1949.

1915. Stack, J. K.: Shoulder pain, Indust. Med. 19: 485 (Oct.) 1950.

1916. Stack, J. K., and Chasten, S.: Intra-articular lesions caused by fat pad hypertrophy, Am. J. Surg. 78: 570 (Nov.) 1949.

- 1918. Stahmer, A. H.: The use of physostigmine and foreign protein therapy in arthritis and related conditions, Wisconsin M. J. 49: 1020 (Nov.) 1950.
- 1919. Stammers, F. A. R.: Pain in the upper limb from mechanisms in the costoclavicular space, Lancet 1: 603 (Apr.) 1950.
- 1920. State, D., and Wangensteen, O. H.: Procaine intravenously in treatment of delayed serum sickness, J. A. M. A. 130: 990 (Apr.) 1946. Correction 131: 245 (May) 1946.
- 1921. Staub, P. L., Menthe, J. W., Nelson, S. S., and Cohn, H.: Excretion of 11-oxycorticosteroids in paraplegic and rheumatoid arthritic patients, J. Clin. Investigation 29: 349 (Mar.) 1950.
- 1922. Staub, P. L.: Subcutaneous cysts of rheumatoid arthritis, New York State J. Med. 49: 1566 (July) 1949.
- 1923. Stecher, R. M.: Heberden's nodes; their relation to other degenerative joint diseases, Arch. Phys. Med. 27: 409 (July) 1946.
- 1924. Stecher, R. M.: The riddle of rheumatoid arthritis, Practitioner 162: 127 (Feb.) 1949.
- 1925. Stecher, R. M.: Heberden's nodes; the clinical characteristics of osteoarthritis of the fingers, Ann. Rheumat. Dis. 7: 1 (Mar.) 1948.
- 1926. Stecher, R. M., Beard, E. E., and Hersh, A. H.: Heberden's nodes; the relationship of the menopause to degenerative joint disease of the fingers, J. Lab. and Clin. Med. 34: 1193 (Sept.) 1949.
- 1927. Stecher, R. M., and Hauser, H.: Ankylosing spondylitis; report of occurrence in 2 brothers, Am. J. Roentgenol. 56: 601 (Nov.) 1946.
- 1928. Stecher, R. M., and Hauser, H.: Heberden's nodes; VII. The roentgenological and clinical appearance of degenerative joint disease of the fingers, Am. J. Roentgenol. 59: 326 (Mar.) 1948.
- 1929. Stecher, R. M., Hersh, A. H., and Solomon, W. M.: The heredity of gout and its relationship to familial hyperuricemia, Ann. Int. Med. 31: 595 (Oct.) 1949.
- 1930. Stecher, R. M., and Karnosh, L. J.: Heberden's nodes; effect of nerve injury upon formation of degenerative joint disease of fingers, Am. J. M. Sc. 213: 181 (Feb.) 1947.
- 1931. Steck, I. E., Joseph, N. R., and Reed, C. I.: The pH of the synovial fluid in the anaesthetized dog under treatment with metrazol or insulin, J. Bone and Joint Surg. 30A: 500 (Apr.) 1948.
- 1932. Steck, I. E., Montgomery, M. M., Reed, C. I., and Joseph, N. R.: Influence of adrenocorticotrophic hormone (ACTH) on differences of potential between synovial fluid and skin in rheumatoid arthritis, J. Appl. Physiol. 3: 84 (Aug.) 1950.
- 1933. Stefanini, M., Roy, C. A., Zannos, L., and Dameshek, W.: Therapeutic effect of pituitary adrenocorticotropic hormone (ACTH) in case of Henoch-Schönlein vascular (anaphylactoid) purpura, J. A. M. A. 144: 1372 (Dec.) 1950.
- 1934. Stein, I.: Painful conditions of the shoulder joint, Physiotherapy Rev. 28: 275 (Nov.-Dec.) 1948.
- 1935. Stein, I., and Bartlett, A. G.: Interference dissociation—early finding in acute rheumatic fever, Am. J. M. Sc. 211: 686 (June) 1946.
- 1936. Steinberg, C. L.: Brucellosis as a cause of sacroiliac arthritis; a study of its relationship to rheumatoid spondylitis, J. A. M. A. 138: 15 (Sept.) 1948.
- 1937. Steinberg, C. L.: Vitamin E and collagen in the rheumatic diseases, Ann. New York Acad. Sc. 52: 380 (Oct.) 1949.
- 1938. Steinbrocker, O.: Therapeutic results in rheumatoid arthritis, J. A. M. A. 131: 189 (May) 1946.
- 1939. Steinbrocker, O.: Shoulder-hand syndrome; associated painful homolateral disability of shoulder and hand with swelling and atrophy of hand, Am. J. Med. 3: 402 (Oct.) 1947.

- 1940. Steinbrocker, O.: Pitfalls in the use of analgesic injections for painful musculoskeletal disorders, Anesth. and Analg. 27: 1 (Jan.-Feb.) 1948.
- 1941. Steinbrocker, O.: A simple pressure gauge for measured palpation in physical diagnosis and therapy, Arch. Phys. Med. 30: 289 (May) 1949.
- 1942. Steinbrocker, O.: Some simple diagnostic measures in neuromuscular and articular pain, with special reference to differential palpation, Am. Pract. 3: 723 (Aug.) 1949.
- 1943. Steinbrocker, O., and Blazer, A.: Therapeutic score card for rheumatoid arthritis; standardized method of appraising results of treatment, New England J. Med. 235: 501 (Oct.) 1946.
- 1944. Steinbrocker, O., and Lapin, L.: Reflex dystrophy in the extremities, New York Med. 5: 15 (Aug. 20) 1949.
- 1945. Steinbrocker, O., Spitzer, N., and Friedman, H. H.: The shoulder-hand syndrome in reflex dystrophy of the upper extremity, Postgrad. Med. 3: 359 (May) 1948.
- 1946. Steinbrocker, O., Spitzer, N., and Friedman, H. H.: The shoulder-hand syndrome in reflex dystrophy of the upper extremity, Ann. Int. Med. 29: 22 (July) 1948.
- 1947. Steinbrocker, O., Spitzer, N., and Friedman, H. H.: The treatment of the shoulder-hand syndrome (reflex dystrophy of the upper extremity), with special reference to sympathetic block; a preliminary report, Anesth. and Analg. 27: 273 (Sept.-Oct.) 1948.
- 1948. Steinbrocker, O., Traeger, C. H., and Batterman, R. C.: Therapeutic criteria in rheumatoid arthritis, J. A. M. A. 140: 659 (June) 1949.
- 1949. Steindler, A.: Arthrogryposis, J. Internat. Coll. Surgeons 12: 21 (Jan.-Feb.) 1949.
- Steiner, G., and Chason, J. L.: Differential diagnosis of rheumatoid arthritis by biopsy of muscle, Am. J. Clin. Path. 18: 931 (Dec.) 1948.
- Steiner, G., Freund, H. A., Leichtentritt, B., and Maun, M. E.: Lesions of skeletal muscles in rheumatoid arthritis; nodular polymyositis, Am. J. Path. 22: 103 (Jan.) 1946.
- 1952. Stenn, F., and Myers, C.: Penicillin in cinchophen-induced agranulocytosis, Am. Pract. 1: 164 (Nov.) 1946.
- 1953. Stephens, C. A. L., Jr., Borden, A. L., Holbrook, W. P., and Hill, D. F.: Use of folic acid in treatment of anemia of rheumatoid arthritis; preliminary report, Ann. Int. Med. 27: 420 (Sept.) 1947.
- 1954. Stephens, C. A. L., Jr., and Holbrook, W. P.: Masked collagen disease, Arizona Med. 6: 21 (Nov.) 1949.
- 1955. Stephens, C. A. L., Jr., Wallraff, E. B., Bordon, A. L., Brodie, E. C., Holbrook, W. P., Hill, D. F., Kent, L., and Kemmerer, A. R.: Apparent free histidine plasma and urine values in rheumatoid arthritis treated with cortisone and ACTH, Proc. Soc. Exper. Biol. and Med. 74: 275 (June) 1950.
- 1956. Stephens, F. E., and Kerby, J. P.: Hereditary Legg-Calve-Perthes disease, J. Hered. 37: 153 (May) 1946.
- 1957. Steven, G. D.: X-ray appearances in chronic rheumatism, Ann. Rheumat. Dis. 6: 1 (Mar.) 1947.
- 1958. Steven, G. D., and Forestier, J.: Discussion on diagnostic radiology in rheumatic disease, Proc. Roy. Soc. Med. 42: 354 (May) 1949.
- 1959. Stevenson, E. M.: Scalenus anticus syndrome, Memphis M. J. 23: 138 (Aug.) 1948.
- 1960. Stevenson, T. W.: Synovitis of wrist, Plast. and Reconstruct. Surg. 2: 443 (Sept.) 1947.
- 1961. Stewart, H. J.: Heart in rheumatic fever, M. Clin. North America 30: 510 (May) 1946.
- 1962. Stewart, M. J.: Benign giant-cell synovioma and its relation to "xanthoma," J. Bone and Joint Surg. 30B: 522 (Aug.) 1948.
- 1963. Stewart, M. J., and Wright, C. J. E.: A recurrent benign giant-cell synovioma of tendon-sheath of 34 years' duration, Brit. J. Surg. 37: 370 (Jan.) 1950.
- 1964. Stinchfield, F. E., and Carroll, R. E.: Vitallium-cup arthroplasty of hip joint; end-result study, J. Bone and Joint Surg. 31A: 628 (July) 1949.

- 1965. Stinchfield, F. E., and Carroll, R. E.: Arthroplasties of the hip, New York State J. Med. 49: 159 (Jan.) 1949.
- 1966. Stock, J. P. P., and McClure, E. C.: Pregnenolone in the treatment of rheumatoid arthritis, Lancet 2: 125 (July) 1950.
- 1967. Stollerman, G. H., and Bernheimer, A. W.: Inhibition of streptolysin S by serum of patients with rheumatic fever and acute streptococcal pharyngitis, J. Clin. Investigation 29: 1147 (Sept.) 1950.
- 1968. Stollerman, G. H., Bernheimer, A. W., and MacLeod, C. M.: The association of lipoproteins with the inhibition of streptolysin S by serum, J. Clin. Investigation 29: 1636, 1950.
- 1969. Stone, R. E., Spies, T. D., and Niedermeier, W.: Rheumatoid arthritis; partial rehabilitation by interval therapy with ACTH and cortisone, Lancet 2: 555 (Nov.) 1950.
- 1970. Storey, J.: Some factor predisposing to juvenile rheumatic fever in Sydney, M. J. Australia 1: 492 (Apr.) 1948.
- 1971. Stork, W. J., and Fleet, C. W.: Tropical yaws; some clinical and roentgenological observations, M. Rec. and Ann. 41: 222 (July) 1947.
- 1972. Straight, W. M.: Periarteritis nodosa; a review with the presentation of 7 cases, Bull. School Med. Univ. Maryland 34: 11 (July) 1949.
- 1973. Straith, C. L., and Lewis, J. R., Jr.: Complete bilateral bony ankylosis of the temporomandibular joint, Alexander Blain Hosp. Bull. 6: 124 (Nov.) 1947.
- 1974. Strakosch, E. A.: Serum sickness-like reactions from penicillin, Rocky Mountain M. J. 43: 558 (July) 1946.
- 1975. Strakosch, E. A.: Acute lupus erythematosus disseminatus treated with penicillin; report of case, Arch. Dermat. and Syph. 54: 197 (Aug.) 1946.
- 1976. Strazza, J. A., Jr.: Delayed sensitization to penicillin similar to serum sickness, J. A. M. A. 130: 1071 (Apr.) 1946.
- 1977. Strazza, J. A., Jr.: Treatment of rheumatoid arthritis with pregnenolone, J. M. Soc. New Jersey 47: 472 (Oct.) 1950.
- 1978. Strong, J. A.: Generalized myositis fibrosa; case report, Ann. Rheumat. Dis. 8: 158 (June) 1949.
- 1979. Strong, J. M.: Fibrositis and segmental neuralgia, Ohio State M. J. 46: 554 (June) 1950.
- 1979a. Stryker, G. V., Tweedal, D. C., and O'Connor, W. B.: Bistrimate therapy in sclero-derma, J. Invest. Dermat. 11: 399 (Dec.) 1948.
- 1980. Stuart, A. M.: Diagnosis and treatment of psoriasis, M. Press 216: 362 (Nov.) 1946.
- 1981. Stuart, B. M., and Pullen, R. L.: Typhoid; clinical analysis of 360 cases, Arch. Int. Med. 78: 629 (Dec.) 1946.
- 1982. Stuart, F. W., and Rose, G. K.: Ankylosing spondylitis treated by osteotomy of the spine, Brit. M. J. 1: 165 (Jan.) 1950.
- 1983. Stuck, W. G.: Surgical treatment of degenerative arthritis of hip, South. M. J. 42: 1021 (Dec.) 1949.
- 1984. Sugar, H. S., and Waddell, W. W.: Ochronosis-like pigmentation associated with use of atabrine, Illinois M. J. 89: 234 (May) 1946.
- 1985. Sugarman, H., and Baltzan, D. M.: Primary splenic neutropenia with rheumatoid arthritis (Felty's syndrome), Canad. M. A. J. 63: 72 (July) 1950.
- 1986. Sulkin, S. E., Pike, R. M., and Coggeshall, H. C.: Specificity of differential sheep cell agglutination test in rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 70: 475 (Mar.) 1949.
- 1987. Sullivan, C. J., Parker, T. W., and Hibbert, R. W.: Prevention by sodium salicylate of arteritis in experimental allergic state, Proc. Soc. Exper. Biol. and Med. 67: 508 (Apr.) 1948.
- 1988. Sumner, J. W., Jr.: Epidural abscess secondary to brucellosis ("Brucella suis"), U. S. Armed Forces M. J. 1: 218 (Feb.) 1950.

1989. Summers, V. K.: Nervous manifestations of periarteritis nodosa, Lancet 1: 1148 (June) 1950.

1990. Sundberg, R. D., and Lick, N. B.: "L.E." cells in the blood in acute disseminated lupus erythematosus, J. Invest. Dermat. 12: 83 (Feb.) 1949.

1991. Sunde, H.: Dermatomyositis in children, Acta pædiat. 37: 287, 1949.

1992. Sundelin, F.: Investigations of cerebrospinal fluid in cases of rheumatoid arthritis, Am. J. Med. 2: 579 (June) 1947.

1993. Sutherland, J. M.: Two cases of periarteritis nodosa; with observations on aetiology, diagnosis, and treatment, Brit. M. J. 1: 832 (May) 1948.

1994. Sutro, C. J.: Hypermobility of bones due to "overlengthened" capsular and ligamentous tissues; cause for recurrent intra-articular effusions, Surgery 21: 67 (Jan.) 1947.

 Sutro, C. J., and Anderson, M. E.: Alkaptonuric arthritis; cause for free intra-articular bodies, Surgery 22: 120 (July) 1947.

1996. Sutro, C. J., and Gladstone, H.: Tuberculosis of the bones of the hip joint, Bull. Hosp. Joint Dis. 10: 20 (Apr.) 1949.

1997. Svartz, N.: The effect of ACTH on the agglutination with sensitized red sheep cells in rheumatoid arthritis, Acta med. Scandinav., supp. 246: 240, 1950.

1998. Svartz, N., and Olhagen, B.: Electrophoretic analysis of proteins in articular rheumatism. Acta med. Scandinav. (Supp. 206) 130: 456, 1948.

1999. Svartz, N., and Schlossmann, K.: The agglutinating factor for sensitized sheep erythrocytes in serum and joint fluid from rheumatoid arthritis patients, Ann. Rheumat. Dis. 9: 377 (Dec.) 1950.

2000. Swaim, L. T.: Problem of chronic rheumatism, Ann. Rheumat. Dis. 5: 192 (Dec.) 1946.
2001. Swaim, L. T.: Role of physical therapy in rheumatic disease, Practitioner 158: 191
(Mar.) 1947.

2002. Swanson, C. A., and Delaney, A. J.: Discussion of Reiter's syndrome, with report of case, U. S. Nav. M. Bull. 48: 503 (July-Aug.) 1948.

2003. Swanson, J. N.: Value of repeated colloidal gold tests, Ann. Rheumat. Dis. 8: 232 (Sept.) 1949.

2004. Swart, H. A.: De Quervain's disease in mother and daughter, West Virginia M. J. 46: 123 (May) 1950.

2005. Sweeney, A. R., Jr., and Baggenstoss, A. H.: Pulmonary lesions of periarteritis nodosa, Proc. Staff Meet., Mayo Clin. 24: 35 (Jan.) 1949.

2006. Sweet, L. K., Dowling, H. F., and Howell, M. J.: Acute meningococcemia, J. Pediat. 30: 438 (Apr.) 1947.

 Sweigert, C. F., Turner, J. W., and Gillespie, J. B.: Clinical and roentgenologic aspects of coccidioidomycosis, Am. J. M. Sc. 212: 652 (Dec.) 1946.

 Swenson, L. L.: Osteochondritis dissecans and osteochondromatosis, J. Michigan M. Soc. 47: 728 (July) 1948.

2009. Swenson, L. L.: Tennis elbow, J. Michigan M. Soc. 48: 997 (Aug.) 1949.

2010. Swift, H. F.: Medical progress; progress in management of rheumatic fever, New York Med. 2: 15 (Dec.) 1946.

 Swift, H. F.: Relationship of streptococcal infections to rheumatic fever, Am. J. Med. 2: 168 (Feb.) 1947.

2011a. Swift, H. F.: Rheumatic fever, Ann. Int. Med. 31: 715 (Nov.) 1949.

2012. Swift, W. E.: Treatment of tuberculosis of the spine in children, Quart. Bull., Sea View Hosp. 8: 360 (Oct.) 1946.

2013. Swyer, G. I. M.: Antihistamine effect of sodium salicylate and its bearing upon skindiffusing activity of hyaluronidase, Biochem. J. 42: 28, 1948.

2014. Swyer, G. I. M.: Failure of in vitro inhibition of hyaluronidase by salicylates, Biochem. J. 42: 32, 1948.

2015. Sylvest, O.: Are rheumatic fever and rheumatoid arthritis accompanied by haemolytic streptococcal bacteriaemia? Ann. Rheumat. Dis. 7: 216 (Dec.) 1948.

- 2016. Sylvest, O., and Hvid-Hansen, N.: Investigations of creatine excretion in urine of 38 untreated ambulant male patients with fibrositis, and 2 healthy men, Ann. Rheumat. Dis. 9: 241 (Sept.) 1950.
- 2017. Sylvester, D. G. H.: Epidemic of benign dry pleurisy, Brit. M. J. 2: 653 (Sept.) 1950.
- 2018. Szucs, M. M.: Succinate-salicylate therapy in arthritis, Ohio State M. J. 43: 1035 (Oct.) 1947.
- 2019. Talbott, J. H.: Medical progress; gout and gouty arthritis, New York Med. (no. 8) 4: 17 (Apr.) 1948.
- 2020. Talbott, J. H.: Diagnosis and treatment of gouty arthritis, Postgrad. Med. 5: 386 (May) 1949.
- 2021. Talbott, J. H.: The diversity of gouty arthritis and its complications, Ann. Int. Med. 31: 555 (Oct.) 1949.
- 2022. Talbott, J. H., Bishop, C., and Garner, W.: A study of labeled uric acid in gouty and non-gouty subjects. Tr. A. Am. Physicians 63: 201, 1950.
- 2023. Talbott, J. H., and Lockie, L. M.: Gouty arthritis, Ciba Clin. Symposia 2: 319 (Dec.) 1950.
- 2024. Talkov, R. H., Ropes, M. W., and Bauer, W.: The value of enteric-coated aspirin, New England I. Med. 242: 19 (Jan.) 1950.
- 2025. Tanberg, A.: Initial symptoms in spondylarthritis ankylopoietica, Rheumatism 6: 127 (July) 1950.
- 2026. Taran, L. M.: Treatment of acute rheumatic fever and acute rheumatic heart disease, Am. J. Med. 2: 285 (Mar.) 1947.
- 2027. Taran, L. M.: A therapeutic regimen for acute heart disease in children, J. Pediat. 33: 226 (Aug.) 1948.
- 2028. Taran, L. M., Jablon, J. M., and Weyr, H. N.: Immunologic studies in rheumatic fever; antistreptolysin patterns in rheumatic children, J. Immunol. 53: 381 (Aug.) 1946.
- 2029. Taran, L. M., and Szilagyi, N.: The duration of the electrical systole (Q-T) in acute rheumatic carditis in children, Am. Heart J. 33: 14 (Jan.) 1947.
- 2030. Taran, L. M., and Szilagyi, N.: Effect of oxygen therapy on the electrical sequence of events in the cardiac cycle in children with acute rheumatic carditis, Am. J. Med. 5: 392 (Sept.) 1948.
- 2031. Tarlov, I. M.: Cysts (perineurial) of the sacral roots; another cause (removable) of sciatic pain, J. A. M. A. 138: 740 (Nov.) 1948.
- 2032. Tarsy, J. M.: Bicipital syndromes and their treatment, New York State J. Med. 46: 996 (May) 1946.
- 2033. Tavernier, L.: Surgical treatment of degenerative arthritis of the hip; articular denervation, Rheumatism 4: 176 (Apr.) 1948.
- 2034. Taylor, A. W., and Jacoby, N. M.: Acute polyarteritis nodosa in childhood, Lancet 2: 792 (Oct.) 1949.
- 2035. Tegner, W.: Fibrositis, Practitioner 157: 446 (Dec.) 1946.
- 2036. Tegner, W. S.: Treatment of rheumatoid arthritis, Lancet 1: 469 (Mar.) 1948.
- 2037. Tegner, W. S.: Lesions of shoulder, J. A. M. A. 141: 835 (Nov.) 1949.
- 2038. Tegner, W. S., O'Neill, D., and Kaldegg, A.: Psychogenic rheumatism, Brit. M. J. 2: 201 (July) 1949.
- 2039. Teilum, G.: Pathogenetic studies on lupus erythematosus disseminatus and related diseases, Acta med. Scandinav. 123: 126, 1946.
- 2040. Teilum, G.: Hyperglobulinemia, periarterial fibrosis of the spleen and the wire loop lesion in disseminated lupus erythematosus in relation to allergic pathogenesis, Am. J. Path. 24: 409 (Mar.) 1948.
- 2041. Teilum, G., Engbaek, H. C., and Simonsen, M.: Effects of cortisone on plasma cells and reticulo-endothelial system in hyperimmunized rabbits, Acta endocrinol. 5: 181, 1950.

- 2042. Telford, E. D., and Mottershead, S.: The costoclavicular syndrome, Brit. M. J. 1: 325 (Mar.) 1947.
- 2043. Temple, H. L., and Jaspin, G.: Hypertrophic osteoarthropathy, Am. J. Roentgenol. 60: 232 (Aug.) 1948.
- 2044. Templeton, W. C.: Meningitis with multiple pyoarthritis (meningococcal), J. Roy. Army M. Corps 88: 227 (June) 1947.
- 2045. Terhune, S. R.: Apparatus for correction of flexion deformity of the knee, J. Bone and Joint Surg. 30A: 244 (Jan.) 1948.
- 2046. Terry, L. L., and London, F.: Effects of Reichstein's compound S, pregnenetriolene acetate and 17-alpha-hydroxyprogesterone in rheumatoid arthritis, Proc. Soc. Exper. Biol. and Med. 73: 251 (Feb.) 1950.
- 2047. Thibodeau, A. A., and McCombs, R. P.: Backache, Bull. New England M. Center 11: 34 (Feb.) 1949.
- 2048. Thoma, K. H.: Ankylosis of mandibular joint, Am. J. Orthodontics (Oral Surg. Sect.) 32: 259 (May) 1946.
- 2049. Thomas, E. W. P., and Rook, A. J.: Syphilitic bursitis with report of a case, Lancet 2: 1221 (Dec.) 1949.
- 2050. Thomas, R. B., and Meyer, E.: Penicillin in the treatment of gonorrhea; results with 675 women, Cincinnati J. Med. 27: 108 (Feb.) 1946.
- Thompson, R. G., White, C. B., and Hailey, H.: Keratosis blennorrhagica; response to streptomycin; report of a case. Arch. Dermat. and Syph. 59: 284 (Mar.) 1949.
- 2052. Thompson, R. T., and Moses, F. E.: Thermostable inhibition of bacterial hyaluronidases by serum of normal human beings, Science 110: 70 (July) 1949.
- Thompson, W. A. L., and Ingersoll, R. E.: Osteotomy for correction of deformity in Marie-Strümpell arthritis, Surg., Gynec. and Obst. 90: 552 (May) 1950.
- 2054. Thomson, G. R.: Treatment of Dupuytren's contracture with vitamin E, Brit. M. J. 2: 1382 (Dec.) 1949.
- 2055. Thorn, G. W., and Bayles, T. B.: Current therapeutics; XXII. Pituitary adrenal function and rheumatic disease, Practitioner 163: 365 (Oct.) 1949.
- 2056. Thorn, G. W., Bayles, T. B., Massell, B. F., Forsham, P. H., Hill, S. R., Smith, S., III, and Warren, J. E.: Medical progress; studies on the relation of pituitary-adrenal function to rheumatic disease, New England J. Med. 241: 529 (Oct.) 1949.
- 2057. Thorn, G. W., Forsham, P. H., Frawley, T. F., Hill, S. R., Jr., Roche, M., Staehelin, D., and Wilson, D. L.: Medical progress; the clinical usefulness of ACTH and cortisone, New England J. Med. 242: 783 (May) 1950; 824 (May) 1950; 865 (June) 1950.
- 2058. Threadgill, F. D.: Causalgic state; early and fixed lesions, M. Ann. District of Columbia 14: 544 (Dec.) 1945.
- 2059. Throm, U. L., II: Reiter's disease with keratosis blennorrhagica, Mil. Surgeon 105: 287 (Oct.) 1949.
- 2060. Tillis, H. H.: Treatment of rheumatoid arthritis by the general practitioner, J. M. Soc. New Jersey 47: 475 (Oct.) 1950.
- 2061. Tippett, G. O.: Diseases of the sacro-iliac joint, M. Press 221: 312 (Mar.) 1949.
- 2062. Toone, E. C., Jr.: Rheumatoid spondylitis; observations on the incidence and response to therapy among veterans of the recent war, Ann. Int. Med. 30: 733 (Apr.) 1949.
- 2063. Torrance, C. C.: Low back pain, Mississippi Valley M. J. 68: 112 (Oct.) 1946.
- 2064. Toumey, J. W.: Intervertebral disk protrusion; selection of cases—type of surgery—after-care, S. Clin. North America 30: 941 (June) 1950.
- Traeger, C. H.: Use of vitamins in treatment of chronic arthritis, M. Clin. North America 30: 616 (May) 1946.
- 2066. Traut, E. F.: Use and abuse of physical therapy in treatment of arthritis, Illinois M. J. 92: 238 (Oct.) 1947.

- Traut, E. F., and Matousek, F. L.: The relation of ascorbic acid to chronic arthritis, Illinois M. J. 95: 38 (Jan.) 1949.
- 2068. Tripi, H. B., Gardner, G. M., and Kuzell, W. C.: Effects of temperature and ultraviolet light on experimental polyarthritis of rats, Proc. Soc. Exper. Biol. and Med. 70: 45 (Jan.) 1949.
- 2069. Tripi, H. B., and Kuzell, W. C.: Production of experimental polyarthritis by pleuro-pneumonia-like (L4) organisms in rats and preliminary results on protective effects of gold product, Stanford M. Bull. 5: 98 (May) 1947.
- 2070. Tripi, H. B., Kuzell, W. C., and Gardner, G. M.: Thiouracil administration and thyroidectomy in experimental polyarthritis of rats, Ann. Rheumat. Dis. 8: 125 (June) 1949.
- 2071. Tucker, F. R.: The use of radioactive phosphorus in the diagnosis of avascular necrosis of the femoral head, J. Bone and Joint Surg. 32B: 100 (Feb.) 1950.
- 2072. Tucker, H. A.: Surgical treatment of inguinal lymphogranuloma venereum; analysis of 613 consecutive cases in the male, Am. J. Syph., Gonor. and Ven. Dis. 30: 495 (Sept.) 1946.
- 2073. Tucker, J. L., and Tepper, W. R.: Intra-articular penicillin treatment of suppurative arthritis in infants and children, J. Pediat. 29: 711 (Dec.) 1946.
- 2074. Tumen, H. J., and Yaskin, J. C.: Backache due to intra-abdominal disease, Gastro-enterology 7: 294 (Sept.) 1946.
- 2075. Tumulty, P. A., and Harvey, A. M.: Clinical course of disseminated lupus erythematosus; evaluation of Osler's contributions, Bull. Johns Hopkins Hosp. 85: 47 (July) 1949.
- Turner, J. P., and Schmidt, F. R.: Treatment of scleroderma with procaine; report of cases, J. A. M. A. 144: 1560 (Dec.) 1950.
- 2077. Twiss, J. R., and Douglas, A. H. R.: Reiter's disease; a report of 2 cases, Ann. Int. Med. 24: 1043, 1946.
- 2078. Tyson, T. L., Holmes, H. H., and Ragan, C.: Copper therapy of rheumatoid arthritis, Am. J. M. Sc. 220: 418 (Oct.) 1950.
- 2079. Tytell, A. A., and Hewson, K.: Production, purification and some properties of Cl. histolyticum collagenase, Proc. Soc. Exper. Biol. and Med. 74: 555, 1950.
- 2080. Ude, W. H.: Osteitis condensans ilii; the possible relationship to juvenile epiphysitis, Journal Lancet 70: 81 (Feb.) 1950.
- 2081. Ulmer, J. L., and Mayfield, F. H.: Causalgia; study of 75 cases, Surg., Gynec. and Obst. 83: 789 (Dec.) 1946.
- 2082. Umansky, A. L., Schlesinger, P. T., and Greenberg, B. B.: Tuberculous dactylitis in adult, Arch. Surg. 54: 67 (Jan.) 1947.
- 2083. Unger, P. N., Zuckerbrod, M., Beck, G. J., and Steele, J. M.: Amyloidosis in rheumatoid arthritis; a report of 10 cases, Am. J. M. Sc. 216: 51 (July) 1948.
- 2084. Upshaw, J. E., and Bickel, W. H.: Tuberculosis of the hip, Minnesota Med. 31: 384 (Apr.) 1948.
- 2085. Uyeda, I.: Rheumatic heart disease; a study of 167 cases among 12,317 autopsies performed at Charity Hospital in New Orleans during 10 years, New Orleans M. and S. J. 98: 271 (Dec.) 1945.
- 2086. Valentine, M.: Aetiology of fibrositis; a review, Ann. Rheumat. Dis. 6: 241 (Dec.) 1947.
- 2087. van der Horst, L.: Rheumatism and psychosis, Digest Neurol. and Psychiat., Inst. of Living 15: 399 (July) 1947.
- 2088. Van Wagenen, W. P.: Intangible factors in the treatment of patients with low back pain, with special reference to industrial patients, New York State J. Med. 47: 2683 (Dec.) 1947.
- 2089. Van Wyk, J. J., and Hoffmann, C. R.: Periarteritis nodosa; case of fatal exfoliative

dermatitis resulting from "dilantin sodium" sensitization, Arch. Int. Med. 81: 605 (May) 1948.

2090. Vasko, J. R.: Calcareous tendinitis of flexor tendon of finger; report of case, J. Bone and Joint Surg. 28: 638 (July) 1946.

2091. Vaughan, C. E., and Stapleton, J. G.: Osteochondritis dissecans of ankle with reports of 4 proved cases, Radiology 49: 72 (July) 1947.

2092. Venning, E. H., Kazmin, V. E., Ripstein, M., McAlpine, H. T., and Hoffman, M. M.: Effect of adrenocorticotropin on excretion of adrenal metabolites in normal human subjects, J. Clin. Endocrinol. 10: 583 (June) 1950.

2093. Verstandig, C. C.: Valvular heart disease (rheumatic) in rejectees; survey of 100,000 cardiac examinations performed at New Haven Recruiting and Induction Station, New Haven, Connecticut, Connecticut M. J. 10: 304 (Apr.) 1946.

2094. Vesey, J. M., and Nelson, H. G.: Acute disseminated lupus erythematosus; report of disease in Negro male, Ann. Int. Med. 32: 565 (Mar.) 1950.

2095. Vinke, T. H., and Downing, H. F.: Salmonella infection involving the knee joint; report of case, J. Bone and Joint Surg. 29: 232 (Jan.) 1947.

2096. Von Glahn, W. C.: Pathology of rheumatism, Am. J. Med. 2: 76 (Jan.) 1947.

2097. Voshell, A. F., and Appleby, G. S.: Osteoid-osteoma associated with myositis ossifians; case report, Bull. School Med. Univ. Maryland 30: 140 (Jan.) 1946.

2098. Wagener, H. P.: Retinal lesions in acute disseminate lupus erythematosus, Am. J. M. Sc. 211: 240 (Feb.) 1946.

2099. Waine, H.: The nature of degenerative joint disease, Ann. West. Med. and Surg. 2: 313 (July) 1948.

2100. Waine, H.: Annual review of rheumatic diseases, Arch. Int. Med. 86: 934 (Dec.) 1950.

2101. Waine, H., Baker, F., and Mettier, S. R.: Controlled evaluation of gold therapy in rheumatoid arthritis, California Med. 66: 295 (May) 1947.

2102. Wainger, C. K., and Lever, W. F.: Dermatomyositis; report of 3 cases with post-mortem observations, Arch. Dermat. and Syph. 59: 196 (Feb.) 1949.

2103. Wakim, K. G., Krusen, F. H., and Elkins, E. C.: Effects of artificially induced fever on the circulation in arthritic patients, Arch. Phys. Med. 29: 274 (May) 1948.

2104. Waksman, B. H., and Mason, H. L.: The antigenicity of collagen, J. Immunol. 63: 427 (Dec.) 1949.

2105. Walker, E. R. C.: Psychological and social aspects of Sydenham's chorea, Edinburgh M. J. 55: 17 (Jan.) 1948.

2106. Walker, E. R. C.: Treatment of Sydenham's chorea, M. Press 220: 445 (Nov.) 1948.

2107. Walker, P. J.: Physical therapy in arthritis, Ann. West. Med. and Surg. 2: 320 (July) 1948.

2108. Walker, S. A., and Benditt, E. P.: Electrophoretic study of the serum proteins in scleroderma, Proc. Soc. Exper. Biol. and Med. 67: 504 (Apr.) 1948.

2109. Wall, M. J.: Isolation of the virus of lymphogranuloma venereum from 28 patients; relative value of the use of chick embryos and mice, J. Immunol. 54: 59, 1946.

2110. Wallach, E. A., and Burkhart, E. F.: Ehlers-Danlos syndrome associated with the tetralogy of Fallot, Arch. Dermat. and Syph. 61: 750 (May) 1950.

2111. Wallerstein, R., Vallee, B. L., and Turner, L.: Possible relationship of pleuropneumonialike organisms to Reiter's disease, rheumatoid arthritis and ulcerative colitis, J. Infect. Dis. 79: 134 (Sept.-Oct.) 1946.

2112. Walley, J. F. L., and Cooper, T. V.: Case of undulant fever treated by chloramphenicol, Brit. M. J. 2: 265 (July) 1949.

 Wallis, A. D.: Rheumatoid arthritis. II. Non-specific serologic reactions, Am. J. M. Sc. 212: 716 (Dec.) 1946.

2114. Wallis, A. D.: Rheumatoid arthritis. III. The pneumococcus antibodies, Am. J. M. Sc. 212: 718 (Dec.) 1946.

- 2115. Wallis, A. D.: Rheumatoid arthritis: hemolytic streptococcus precipitin reactions, Am. J. M. Sc. 213: 87 (Jan.) 1947.
- 2116. Wallis, A. D.: Rheumatoid arthritis; agglutination of hemolytic streptococci, Am. J. M. Sc. 213: 94 (Jan.) 1947.
- 2117. Wallis, A. D.: The relation of the vascular apparatus to rheumatoid arthritis, South. M. J. 41: 362 (Apr.) 1948.
- 2118. Wallis, A. D.: Serum proteins in rheumatoid arthritis, Ann. Int. Med. 32: 63 (Jan.) 1950.
- 2119. Wallis, A. D.: A theory of the pathogenesis of rheumatoid arthritis, Ann. Rheumat. Dis. 9: 331 (Dec.) 1950.
- 2120. Wallis, A. D., and Horvath, S. M.: Effect of hyper-immune states on human blood pressure response to epinephrine, J. App. Physiol. 1: 856 (June) 1949.
- 2121. Warren, H. A., and Chornyak, J.: Cerebral manifestations of acute rheumatic fever, Arch. Int. Med. 79: 589 (June) 1947.
- 2122. Warren, H. A., Higley, C. S., and Coombs, F. S.: Effect of salicylates on acute rheumatic fever, Am. Heart J. 32: 311 (Sept.) 1946.
- 2123. Warter, P. J., Betts, R. W., and Horoschak, S.: Gastrointestinal tract and nutrition in rheumatoid arthritis, Rev. Gastroenterol. 14: 617 (Sept.) 1947.
- 2124. Warter, P. J., Donio, D. A., and Horoschak, S.: Combined (streptococcus-staphylococcus) antigens in treatment of rheumatoid arthritis, J. M. Soc. New Jersey 44: 441 (Nov.) 1947.
- 2125. Warter, P. J., Drezner, H. L., and Horoschak, S.: The influence of hesperidin-C on abnormal capillary fragility in rheumatoid arthritis patients, Delaware State M. J. 20: 41 (Mar.) 1948.
- 2126. Warthin, T. A.: Reiter's syndrome; a report on 4 patients treated with streptomycin, Am. J. Med. 4: 827 (June) 1948.
- 2127. Warthin, T. A., Cooper, J. F., and Caputi, A. P.: Clubbing of digits, metaplasia of urinary bladder and mucous diarrhea, Arch. Int. Med. 86: 10 (July) 1950.
- 2128. Wartman, W. B., and Hellerstein, H. K.: The incidence of heart disease in 2,000 consecutive autopsies, Ann. Int. Med. 28: 41, 1948.
- 2129. Wassmann, K.: Rheumatoid arthritis and psoriasis; statistical statements, Ann. Rheumat. Dis. 8: 70 (Mar.) 1949.
- 2130. Wasson, V. P., Miley, G. P., and Dunning, P. M.: Ultraviolet blood irradiation therapy (Knott technique) in rheumatic fever in children, Exper. Med. and Surg. 8: 15 (Feb.) 1950.
- 2131. Watkins, A. L.: Physical medicine in the treatment of degenerative joint disease, M. Clin. North America 33: 1313 (Sept.) 1949.
- 2132. Watkins, C. G.: Ratbite fever, J. Pediat. 28: 429 (Apr.) 1946.
- 2133. Watkins, W. W.: "Last-straw" factor in low back disability, with summary of 100 cases examined and evaluated by Medical Advisory Board of Industrial Commission of Arizona, 1934–1943, Radiology 48: 20 (Jan.) 1947.
- 2134. Waxman, A., and Geshelin, H.: Boxer's bursitis, California Med. 69: 203 (Sept.) 1948.
- 2135. Webb, E. M., and Davis, E. W.: Causalgia; a review, California Med. 69: 412 (Dec.) 1948.
- 2136. Weber, F. P.: Palindromic rheumatism, Lancet 2: 931 (Dec.) 1946.
- 2137. Weber, F. P.: Necrobiotic nodules of rheumatoid arthritis type, with remarks on rheumatoid arthritis, M. Press 219: 484 (June) 1948.
- 2139. Wedderburn, C. C.: Lymphogranuloma venereum, Jamaica M. Rev. 1: 56 (Aug.) 1947.
- 2140. Wedum, B. G., Darley, W., and Rhodes, P. H.: Prevalence of rheumatic heart disease at high altitudes, Am. J. Dis. Child. 79: 205 (Feb.) 1950.
- 2141. Wedum, A. G., and Wedum, B. G.: Serum precipitation reaction in rheumatic fever and in other conditions, Proc. Soc. Exper. Biol. and Med. 61: 432 (Apr.) 1946.

2142. Weeks, K. D., and Smith, D. T.: Lepromin skin tests in Boeck's sarcoid, Am. J. Trop. Med. 25: 519 (Nov.) 1945.

2143. Wegria, R., Weaver, D., and Krakauer, H.: The effect of the ingestion of aluminum hydroxide on the serum salicylate level, New York State J. Med. 49: 658 (Mar.) 1949.

2144. Wegria, R., Fischel, E. E., and Wilson, P. E.: Succinate therapy in acute rheumatic fever, New England J. Med. 239: 117 (July) 1948.

2145. Weinstein, L., Bachrach, L., and Boyer, N. H.: Observations on the development of rheumatic fever and glomerulonephritis in cases of scarlet fever treated with penicillin, New England J. Med. 242: 1002 (June) 1950.

2146. Weinstock, H. L., and Keesal, S.: Lymphogranuloma venereum; report of a case in a child, Urol. and Cutan. Rev. 50: 520 (Sept.) 1946.

2147. Weintraub, H. J., and Bishop, L. F., Jr.: Daily changing picture in case of acute rheumatic carditis, Am. Heart J. 34: 284 (Aug.) 1947.

2148. Weisman, J. C.: Medial femoral triangle of translucency simulating osteochondritis dissecans, Am. J. Roentgenol. 58: 166 (Aug.) 1947.

2149. Weiss, E.: Psychogenic rheumatism, Ann. Int. Med. 26: 890 (June) 1947.

2150. Weiss, T. E.: The basic treatment of rheumatoid arthritis, New Orleans M. and S. J. 101: 496 (Apr.) 1949.

2151. Weller, T. H., Enders, J. F., Buckingham, M., and Finn, J. J., Jr.: The etiology of epidemic pleurodynia; a study of 2 viruses isolated from a typical outbreak, J. Immunol. 65: 337 (Sept.) 1950.

2152. Wells, B. B., Lowrey, R. D., and Seibert, V. E.: Desoxycorticosterone acetate and ascorbic acid in the treatment of rheumatoid arthritis, J. Arkansas M. Soc. 47: 3 (June) 1950.

2153. Wells, P. O.: Osteochondritis of spine, Mil. Surgeon 107: 270 (Oct.) 1950.

2154. Welsh, A. L.: Specificity of streptococci isolated from patients with skin diseases; Studies on pemphigus, dermatitis herpetiformis, lupus erythematosus and erythema multiforme. III. Lupus erythematosus disseminatus, J. Invest. Dermat. 10: 304 (May) 1948.

2155. Welsh, A. L.: Diagnostic test for distinguishing pemphigus, dermatitis herpetiformis, disseminate lupus erythematosus, and erythema multiforme exudativum, J. Invest. Dermat. 11: 19 (July) 1948.

2156. Werblow, S. C.: The value of the electrocardiogram in the diagnosis of early rheumatic heart disease, South. M. J. 40: 443 (May) 1947.

2157. West, E. F.: Role of spinal fusion in arthrogenic sciatica; review of 52 cases, M. J. Australia 2: 711 (Dec.) 1947.

2158. West, H. F.: Actiology of ankylosing spondylitis, Ann. Rheumat. Dis. 8: 143 (June) 1949.

2159. Wheatley, G. M.: Some public health aspects of rheumatic fever; including the present status of organized efforts to control its effects, West Virginia M. J. 43: 57 (Feb.) 1947.

2159a. Wheatley, G. M.: The physician and community action for rheumatic fever, J. Michigan M. Soc. 48: 1128 (Sept.) 1949.

2160. Whipple, R. L., Jr., and Davidson, J. K., III: Acute disseminated lupus erythematosus; report of a case treated with adrenocorticotropic hormone (ACTH) with clinical and metabolic observations and autopsy findings, J. Lab. and Clin. Med. 36: 206 (Aug.) 1950.

2161. White, A. G., Parker, J. G., and Block, F.: Studies on human alcaptonuria; effect of thiouracil, para-aminobenzoic acid and di-iodotyrosine on excretion of homogentisic acid, J. Clin. Investigation 28: 140 (Jan.) 1949.

2162. White, R. K.: Patellectomy; simple and effective treatment for chronic arthritis of knee, Hahneman. Monthly 81: 428 (Oct.) 1946.

- 2163. Whiteleather, J. E., Semmes, R. E., and Murphy, F.: Roentgenographic signs of herniation of cervical intervertebral disk, Radiology 46: 213 (Mar.) 1946.
- 2164. Whitman, J. F., and Karnosh, L. J.: Rheumatic brain disease as a cause of convulsions, Cleveland Clin. Quart. 16: 136 (July) 1949.
- 2165. Wiesel, L. L., Barritt, A. S., Jr., and Stumpe, W. M.: The synergistic action of paraaminobenzoic acid and cortisone in the treatment of rheumatoid arthritis; a preliminary report, Brooklyn Hosp. J. 8: 148, 1950.
- 2166. Wigley, J. E. M., Edmunds, V., and Bradley, R.: Pulmonary fibrosis in scleroderma, Brit. J. Dermat. 61: 324 (Oct.) 1949.
- 2167. Wilkinson, J. F.: Management and treatment of haemophilia, M. Press 218: 481 (Nov.) 1947.
- 2168. Wilkinson, M. C.: Treatment of bone tuberculosis in relation to multiple tuberculous lesions, Proc. Roy. Soc. Med. 39: 712 (Sept.) 1946.
- 2169. Wilkinson, M. C.: Intertrochanteric osteotomy for treatment of tuberculosis of the hip, Proc. Roy. Soc. Med. 40: 238 (Mar.) 1947.
- 2170. Wilmer, H. A., and Elkins, E. C.: Optical goniometer for observing range of motion of joints; preliminary report of new instrument, Arch. Phys. Med. 28: 695 (Nov.) 1947.
- 2171. Willcox, R. R., Findlay, G. M., and Henderson-Begg, A.: Treatment of Reiter's syndrome by gold salts, Brit. M. J. 1: 483 (Apr.) 1947.
- 2172. Williams, A. J.: Rheumatoid (Marie-Strümpell) spondylitis; technique of examination and importance of the costal joints, California Med. 70: 257 (Apr.) 1949.
- 2173. Williams, R. D., and Mahaffey, H. W.: Synovioma; case report with pulmonary metastases that regressed following irradiation, Ohio State M. J. 45: 988 (Oct.) 1949.
- 2174. Willner, P.: Osteochondritis dissecans of elbow, J. Internat. Coll. Surgeons 13: 791 (June) 1950.
- 2175. Wilson, A. P., and Jordon, J. W.: Relationship of chronic discoid and disseminated lupus erythematosus, New York State J. Med. 50: 2449 (Oct.) 1950.
- 2176. Wilson, C. L.: Formation of new bursae with cellophane, J. Bone and Joint Surg. 30A: 195 (Jan.) 1948.
- 2177. Wilson, D.: Epidemic myalgia affecting trapezius muscle, Ann. Rheumat. Dis. 5: 211 (Dec.) 1946.
- 2178. Wilson, G. D.: Fibrositis, South. M. J. 42: 387 (May) 1949.
- 2179. Wilson, J. N.: Prolapsed intervertebral disk after lumbar puncture, Brit. M. J. 2: 1334 (Dec.) 1949.
- 2180. Wilson, M. G.: Susceptibility of the host in rheumatic fever, M. Clin. North America 30: 534 (May) 1946.
- 2181. Wilson, M. G.: Heredity and rheumatic disease, Am. J. Med. 2: 190 (Feb.) 1947.
- 2182. Wilson, M. G., and Lubschez, R.: Studies in ascorbic acid with especial reference to white layer; relation of intake to blood levels in normal children and the effect of acute and chronic illness, J. Clin. Investigation 25: 428 (May) 1946.
- 2183. Wilson, M. G., and Lubschez, R.: Longevity in rheumatic fever, based on the experience of 1,042 children observed over a period of 30 years, J. A. M. A. 138: 794 (Nov.) 1948.
- 2184. Wilson, M. G., and Lubschez, R.: Immunologic and biochemical studies in infants and children with special reference to rheumatic fever; electrophoretic patterns of blood plasma and serum in rheumatic children, Pediatrics 2: 577 (Nov.) 1948.
- 2185. Wilson, P. D., and Straub, L. R.: Operative indications in trauma to the low back, Am. J. Surg. 74: 270 (Sept.) 1947.
- 2186. Wilson, R.: Case of dermatomyositis, Bull. Vancouver M. A. 24: 273 (May) 1948.
- 2187. Winblad, S., and Edström, G.: Studies on the agglutinins against hemolytic streptococci in rheumatic diseases, Acta path. et microbiol. Scandinav. 25: 715, 1948.

2188. Winchester, J. W., and Mekie, E. C.: Tendinitis of flexor carpi ulnaris, Brit. J. Radiol. 20: 482 (Nov.) 1947.

2189. Windholz, F., and Foster, S. E.: Sclerosis of bones in Gaucher's disease, Am. J. Roent-genol. 60: 246 (Aug.) 1948.

2190. Wingfield, W. L., and Toone, E. C., Jr.: Calcinosis; report of a case, Virginia M. Monthly 76: 230 (May) 1949.

2191. Winkelman, N. W., and Moore, M. T.: Disseminated necrotizing panarteritis (peri-arteritis nodosa); a clinicopathologic report, J. Neuropath. and Exper. Neurol. 9: 60 (Jan.) 1950.

2192. Winkler, H.: Mold arthroplasty, North Carolina M. J. 11: 196 (Apr.) 1950.

2193. Winter, C. A., and Flataker, L.: Influence of cortisone and related steroids upon spreading effect of hyaluronidase, Federation Proc. 9: 137, 1950.

2194. Winter, C. A., Silber, R. H., and Stoerk, H. C.: Production of reversible hyperadrenocortinism in rats by prolonged administration of cortisone, Endocrinology 47: 60 (July) 1950.

2195. Withers, R. J. W.: Painful shoulder; review of 100 personal cases with remarks on pathology, J. Bone and Joint Surg. 31B: 414 (Aug.) 1949.

2196. Withers, R. J. W.: Painful shoulder, Ulster M. J. 19: 112 (May) 1950.

2197. Wittkower, E.: Psychological aspects of skin disease, Bull. Menninger Clin. 11: 148 (Sept.) 1947.

2198. Wold, L. E., and Baggenstoss, A. H.: Gastro-intestinal lesions of periarteritis nodosa, Proc. Staff Meet., Mayo Clin. 24: 28 (Jan.) 1949.

2199. Wold, L. E., and Barker, N. W.: Periarteritis nodosa (essential polyarteritis); clinical data on 30 cases proved at necropsy, Minnesota Med. 32: 714 (July) 1949.

2200. Wolf, J.: Larsen-Johansson disease of patella; 7 new case records; its relationship to other forms of osteochondritis; use of male sex hormones as new form of treatment, Brit. J. Radiol. 23: 335 (June) 1950.

2201. Wolf, R. E., Rauh, L. W., and Lyon, R. A.: Prevention of rheumatic recurrences in children by use of sulfathiazole and sulfadiazine, J. Pediat. 27: 516 (Dec.) 1945.

2202. Wolff, E.: Trauma and arthritis; analysis of 162 cases, Indust. Med. 17: 41 (Feb.) 1948.

2203. Wolfson, S. A., and Alter, M. S.: Palindromic rheumatism, Ann. Rheumat. Dis. 7: 156 (Sept.) 1948.

2204. Wolfson, W. Q., and Cohn, C.: The role of the pituitary adrenocorticotrophic hormone (ACTH) and of adrenal cortical steroid hormones in the pathological physiology and experimental therapeutics of clinical gout, Proceedings of the First Clinical ACTH Conference, 1950, The Blakiston Co., Philadelphia, p. 241.

2205. Wolfson, W. Q., Cohn, C., Levine, R., and Huddlestun, B.: The transport and excretion of uric acid in man. III. Physiological significance of the uricosuric effect of

caronamide, Am. J. Med. 4: 774, 1948.

2206. Wolfson, W. Q., Cohn, C., Levine, R., Rosenberg, E. F., and Hunt, H. D.: Liver function and serum protein structure in gout, Ann. Int. Med. 30: 598 (Jan.) 1949.

 Wolfson, W. Q., Cohn, C., and Shore, C.: The renal mechanism for urate excretion in the Dalmatian coach-hound, J. Exper. Med. 92: 121 (Aug.) 1950.

2208. Wolfson, W. Q., Guterman, H. S., Levine, R., Cohn, C., Hunt, H. D., and Rosenberg, E. F.: Endocrine finding apparently characteristic of gout: very low urinary 17-ketosteroid excretion with clinically normal androgenic function, J. Clin. Endocrinol. 9: 497 (June) 1949.

2209. Wolfson, W. Q., Huddlestun, B., and Levine, R.: Transport and excretion of uric acid in man; endogenous uric acid-like chromogen of biologic fluids, J. Clin. Investigation 26: 995 (Sept.) 1947.

2210. Wolfson, W. Q., Hunt, H. D., Cohn, C., Robinson, W. D., and Duff, I. F.: ACTH and colchicine in the clinical treatment of acute gouty arthritis; physiological considerations and review of therapeutic results in 51 attacks, J. Michigan M. Soc. 49: 1058

(Sept.) 1950.

2211. Wolfson, W. Q., Hunt, H. D., Levine, R., Guterman, H. S., Cohn, C., Rosenberg, E. F., Huddlestun, B., and Kadata, K.: The transport and excretion of uric acid in man. V. A sex difference in urate metabolism with a note on clinical and laboratory findings in gouty women, J. Clin. Endocrinol. 9: 749 (Aug.) 1949.

2212. Wolfson, W. Q., and Levine, R.: The transport and excretion of uric acid in man. IV. The renal mechanism for urate excretion, Federation Proc. 7: 136 (Mar.) 1948.

2213. Wolfson, W. Q., Levine, R., and Tinsley, M.: Transport and excretion of uric acid in man; true uric acid in normal cerebrospinal fluid, in plasma, and in ultrafiltrates of plasma, J. Clin. Investigation 26: 991 (Sept.) 1947.

2214. Wood, F. G., and Wilkinson, M. C.: Tomography of the spine in tuberculous diseases,

Brit. J. Radiol. 20: 418 (Oct.) 1947.

2215. Wood, P.: Reiter's disease, Brit. M. J. 2: 309, 1946.

2215a. Wood, P.: Discussion on management of rheumatic fever and its early complications, Proc. Roy. Soc. Med. 63: 195 (Mar.) 1950.

2216. Woodburne, R. T.: Rupture and attritional defects of the supraspinatus tendon; an examination of cadaver material, Univ. Michigan M. Bull. 16: 61 (Mar.) 1950.

2217. Woodhall, B., and Hayes, G. J.: The well-leg-raising test of Fajersztajn in the diagnosis of ruptured lumbar intervertebral disc, J. Bone and Joint Surg. 32A: 786 (Oct.) 1950.

2218. Woodland, R. J. T.: Tuberculous rheumatism; report of a case, Lancet 2: 540 (Oct.) 1947.

2219. Woodmansey, A., and Wilson, J. V.: A method for measuring plasma viscosity and a comparison of plasma viscosity with blood sedimentation rate in rheumatoid arthritis, Ann. Rheumat. Dis. 7: 235 (Dec.) 1948.

2219a. Woodward, T. E., Smadel, J. E., Holbrook, W. A., Jr., and Raby, W. T.: The beneficial effect of chloromycetin in brucellosis, J. Clin. Investigation 28: 968 (Sept.) (pt. 1) 1949.

2220. Woolf, D. L.: Case of calcinosis circumscripta, Ann. Rheumat. Dis. 6: 208 (Dec.) 1947.
2221. Woolsey, R. D., and Coldwater, K. B.: Surgical treatment of intervertebral disk lesions of veterans, J. Missouri M. A. 44: 651 (Sept.) 1947.

2222. Wramner, T.: Neostigmine in treatment of muscle spasm in rheumatoid arthritis, Acta med. Scandinav. 126: 241, 1946.

2223. Wrete, M.: Sensory pathways from shoulder joint, J. Neurosurg. 6: 351 (Sept.) 1949.

2224. Wright, H. P.: Occupational therapy in rheumatoid arthritis, Canad. M. A. J. 56: 313 (Mar.) 1947.

2225. Wright, H. P.: Present status of gold therapy in rheumatoid arthritis, Canad. M. A. J. 59: 359 (Oct.) 1948.

2226. Wright, H. P., and Milnes, S. H.: Simple method of measuring and recording movements in joints, Treat. Serv. Bull. (no. 8) 2: 33 (Oct.) 1947.

2227. Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., and Hill, L. M.: Aureomycin: a new antibiotic with virucidal properties; a preliminary report on successful treatment in 25 cases of lymphogranuloma venereum, J. A. M. A. 138: 408 (Oct.) 1948.

2228. Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., and Hill, L. M.: The treatment of lymphogranuloma venereum and granuloma inguinale in humans with aureomycin, Ann. New York Acad. Sc. 51: 318 (Nov.) 1948.

2229. Wrigley, F.: Reiter's disease, Brit. M. J. 2: 199, 1946.

2230. Wuerthele-Caspe, V., Brodkin, E., and Mermod, C.: Etiology of scleroderma; preliminary clinical report, J. M. Soc. New Jersey 44: 256 (July) 1947.

2231. Wycis, H. T.: Contralateral recurrent herniated disks, Arch. Surg. 60: 274 (Feb.) 1950.

2232. Wylie, P. E.: Subdeltoid bursitis, Mil. Surgeon 105: 237 (Sept.) 1949.

- 2233. Yahraes, Herbert: Rheumatic fever: childhood's greatest enemy, Public Affairs Pamphlet No. 126, New York, Public Affairs Committee, 1947.
- 2234. Yampolsky, J., and Heyman, A.: Penicillin in the treatment of syphilis in children, J. A. M. A. 132: 368 (Oct.) 1946.
- 2235. Yarumian, K., and Kleinerman, J.: Pathogenesis of so-called diffuse vascular or collagen disease, Arch. Int. Med. 83: 1 (Jan.) 1949.
- 2236. Yorden, E., and Kehoe, E. L.: Severe keratosis blennorrhagica complicating Reiter's disease, Mil. Surgeon 105: 466 (Dec.) 1949.
- 2237. Young, B. R.: Roentgen treatment of bursitis of shoulder, Am. J. Roentgenol. 56: 626 (Nov.) 1946.
- 2238. Young, H. H.: Orthopedic aspects of pain in shoulder and arm, S. Clin. North America 26: 834 (Aug.) 1946.
- 2239. Young, J. H.: Recent advances in diagnosis and treatment of lumbar intervertebral disc disease, M. J. Australia 1: 45 (Jan.) 1946.
- 2240. Young, J. H.: Cervical and thoracic intervertebral disk disease, M. J. Australia 2: 833 (Dec.) 1946.
- 2241. Young, R. H.: Protrusion of intervertebral discs, Proc. Roy. Soc. Med. 40: 233 (Mar.) 1947.
- 2242. Young, R. H., and McEwen, E. G.: Bacillary dysentery as cause of Reiter's syndrome (arthritis with nonspecific urethritis and conjunctivitis), J. A. M. A. 134: 1456 (Aug.) 1947.
- 2243. Young, W. R., and Viko, L. E.: Rheumatic fever in school children in Utah, Rocky Mountain M. J. 47: 426 (June) 1950.
- 2244. Youngner, J. S., and Altshuler, C. H.: Failure to relate hyaluronic acid to elevated erythrocyte sedimentation rate in rheumatic diseases, Proc. Soc. Exper. Biol. and Med. 67: 92 (Jan.) 1948.
- 2245. Ytrehus, Ø.: Three cases of Felty syndrome, Acta med. Scandinav. 126: 437, 1947.
- 2246. Yü, T. F., and Gutman, A. B.: Interference of gentisic acid in determination of urinary uric acid after administration of salicylates, Federation Proc. 8: 267 (Mar.) 1949.
- 2247. Zaino, E. C., and Sharnoff, J. G.: A fatal case of allergic dermatitis with manifestations of combined collagen diseases, New York State J. Med. 50: 1261 (May) 1950.
- 2248. Zarafonetis, C. J. D.: Therapeutic possibilities of para-aminobenzoic acid, Ann. Int. Med. 30: 1188 (June) 1949.
- 2249. Zarafonetis, C. J. D., Curtis, A. C., and Gulick, A. E.: Use of para-aminobenzoic acid in dermatomyositis and scleroderma; report of 6 cases, Arch. Int. Med. 85: 27 (Jan.) 1950.
- 2250. Zarafonetis, C. J. D., Grekin, R. H., and Curtis, A. C.: Further studies on the treatment of lupus erythematosus with sodium para-aminobenzoate, J. Invest. Dermat. 11: 359 (Nov.) 1948.
- Zeek, P. M., Smith, C. C., and Weeter, J. C.: Studies on periarteritis nodosa; differentiation between vascular lesions of periarteritis nodosa and of hypersensitivity, Am. J. Path. 24: 889 (July) 1948.
- 2252. Zeiter, W. J., and House, F. B.: Cervical periarthritis; diagnosis and treatment, Cleveland Clin. Quart. 13: 18 (Jan.) 1946; also, Arch. Phys. Med. 27: 162 (Mar.) 1946.
- 2253. Zeller, M.: Rheumatoid arthritis—food allergy as a factor, Ann. Allergy 7: 200 (Mar.-Apr.) 1949.
- 2254. Zewi, M.: Morbus Reiteri, Acta ophth. 25: 47, 1947.
- 2255. Zimmerman, C. E.: Undulant fever, increasing menace to health in Georgia, J. M. A. Georgia 35: 327 (Nov.) 1946.
- 2256. Zinneman, H. H.: Ten cases of amoebiasis with arthritic complaints, Am. J. Digest. Dis. 17: 342 (Oct.) 1950.

Воокз. 1946-1950

AMERICAN HEART ASSOCIATION, INC., AMERICAN COUNCIL ON RHEUMATIC FEVER: Institutional care facilities in the United States for rheumatic fever and rheumatic heart disease (children and adults), 1949, American Heart Association, New York, 44 pp.

BACH, T. F., Editor: Arthritis and related conditions, 1947, F. A. Davis Co., Philadelphia, 472 pp.

BRAILSFORD, J. F.: The radiology of bones and joints, 4th Ed., 1948, J. and A. Churchill, London; Williams and Wilkins Co., Baltimore, 760 pp.

British Rheumatism Association: The scourge of rheumatism: report of a conference held by the British Rheumatism Association, 1949, William Heinemann, Ltd., London, 85 pp.

COLLINS, D. H.: The pathology of articular and spinal disease, 1950, Williams and Wilkins Co., Baltimore, 331 pp.

COPEMAN, W. S. C.: The treatment of rheumatism in general practice, 4th Ed., 1946, William Wood and Co., Baltimore, 264 pp.

COPEMAN, W. S. C., Editor: Textbook of the rheumatic diseases, 1948, E. and S. Livingston, Edinburgh; Williams and Wilkins Co., Baltimore, 612 pp.

CROWE, H. W.: Osteoarthritis of the hipjoint, 1948, Rolls House Publishing Co., Ltd., London, 70 pp.

CYRIAX, J.: Rheumatism and soft tissue injuries, 1947, Paul B. Hoeber, Inc., New York, 410 pp.

DELORIMIER, A. A.: The arthropathies: a handbook of roentgen diagnosis. 2nd Ed., 1949, The Year Book Publishers, Inc., Chicago, 335 pp.

FLETCHER, E.: Medical disorders of the locomotor system including the rheumatic diseases, 1947, Williams and Wilkins Co., Baltimore; E. and S. Livingstone, Edinburgh, 625 pp.

HERNAMAN-JOHNSON, F., and LAW, W. A.: Ankylosing spondylitis: a practical guide to its diagnosis and treatment, 1949, C. V. Mosby Co., St. Louis; Butterworth and Co., Ltd., London, 208 pp.

Holbrook, W. P., Hill, D. F., and Stephens, C. A. L., Jr.: Manual of rheumatic diseases, 1950, Year Book Publishers, Inc., Chicago, 182 pp.

HOLLANDER, J. L., Editor: Comroe's arthritis and allied conditions, 4th Ed., 1949, Lea and Febiger, Philadelphia, 1108 pp.

Kersley, G. D.: The rheumatic diseases, 3d Ed., 1950, Grune and Stratton, Inc., New York, 143 pp.

LEWIN, P.: The back and its disorders, 1948, Whittlesey House Health Series, McGraw-Hill, London, 170 pp.

MARKOVITS, E.: Bone and joint radiology, 1949, Macmillan Co., New York, 446 pp.

STONE, K.: Diseases of the joints and rheumatism, 1947, Grune and Stratton, Inc., New York, 362 pp.

CASE REPORTS

SPONTANEOUS HEMOPNEUMOTHORAX—WITH REFERENCE TO THE USE OF STREPTOKINASE AND STREPTODORNASE *

By Philip N. Jones, Captain, U.S.A.F. (MC), Chanute Air Force Base, Illinois, and Roy S. Bigham, Jr., Captain, U.S.A.F. (MC),

Charlotte, North Carolina

Spontaneous or idiopathic hemopneumothorax is thought to be an unusual and rare occurrence. A review of the literature discloses that there have been about 120 cases recorded. Pitt and Rolleston are usually given credit for publishing the first two comprehensive case reports in 1901. Each author independently reported a case of fatal spontaneous hemopneumothorax. Hartzell in 1942 collected 40 cases and added four of his own. Eidinger and Rubin in 1952 reviewed the literature and found 56 additional cases and added three of their own. In addition to these 103 cases there have been some 17 cases reported in the past two years. E-0

Whereas recovery is usually the rule in simple spontaneous pneumothorax, the mortality rate of spontaneous hemopneumothorax is said to approach 25 per cent, with death usually occurring during the first 24 to 48 hours. The prognosis is excellent provided the patient survives the acute episode. However, blood in the pleural space introduces the possibility of an inexpansible lung because of the deposition and organization of fibrin. A decortication then usually becomes necessary. Thus it is seen that this condition is potentially a grave emergency which requires early and energetic therapy if unnecessary mortality

and morbidity are to be avoided.

The occurrence of spontaneous hemopneumothorax is probably not so rare as the number of case reports would indicate. Many of the authors report multiple cases seen over a period of a relatively few years. There has been a tendency to report only fatal cases, and there must be a large number of cases which have not been published. Any physician actively engaged in the practice of medicine may well be called upon to treat this disease. The concept of treatment of hemothorax has been radically changed during the past few years, largely because of the knowledge gained in treating the vast number of traumatic hemothoraces during World War II.¹⁰

More recently, Tillett and his associates have introduced a new biologic approach to the therapy of clotted hemothorax with the use of streptokinase and streptodornase.^{11, 12} It is the purpose of this paper to review briefly the problem of spontaneous hemopneumothorax and to report a case successfully treated

with these two enzymes.

* Received for publication April 3, 1953. From the Medical Service, U. S. Air Force Hospital, Chanute Air Force Base, Illinois.

CASE REPORT

A 22 year old white airman was admitted to the hospital on October 4, 1952, complaining of severe pain in the left chest. Three days prior to admission he had noted in the general region of the precordium a mild ache having no relation to exertion, respiration or position. The ache gradually subsided. On the day of admission, while eating his breakfast, the patient suddenly developed a severe pain in his left chest. There was no history of any similar episode and no past history suggestive of pneumonia or tuberculosis. He had been in good health prior to this illness, and denied that he had exerted himself in any way.

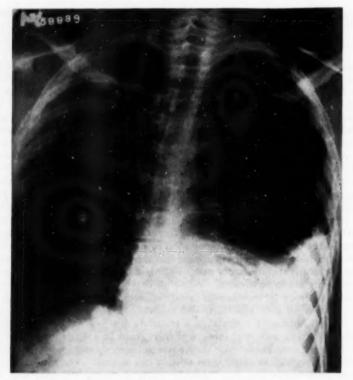


Fig. 1. Chest x-ray, October 4, 1952. Initial film showing left hydropneumothorax.

Physical examination disclosed a well developed, tall, thin white male who appeared to be suffering from severe pain and apprehension. The blood pressure was 106/80 mm. of Hg; temperature, 97.6° F.; pulse, 84; respirations, 15 per minute. Examination of the head and neck revealed no pertinent findings. The trachea was in the midline. There was marked restriction of chest excursions on the left. The left chest was dull to percussion up to the level of the angle of the scapula. The breath sounds were markedly diminished in this same area. The heart size, sounds and rhythm were normal. The abdomen was soft and nontender. The liver and

spleen were not palpable. The remainder of the physical examination was within normal limits.

Laboratory Data: The urinalysis was normal. The red blood cell count was 3,200,000 per cubic millimeter, and there were 10.0 gm. of hemoglobin. The white blood cell count was 17,050, with 56 per cent neutrophils, 41 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The bleeding and coagulation times were normal, the platelet count was 296,000, and the prothrombin time was 14 seconds (control, 13.5 seconds).

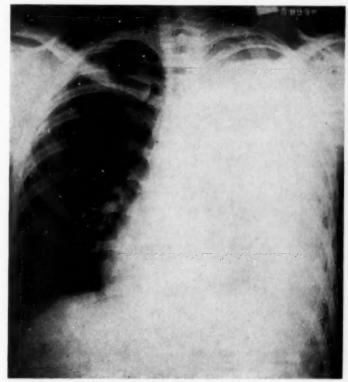


Fig. 2. Chest x-ray, October 20, 1952. Complete obliteration of the left hemithorax by the hemothorax, with displacement of the mediastinum to the right.

The x-ray of the chest on admission revealed a left hydropneumothorax, with about 40 per cent collapse of the left lung (figure 1). A fluid level was noted in the third anterior intercostal space. There was no mediastinal displacement.

A diagnostic thoracentesis was performed and a small amount of fluid resembling whole blood removed. No evidence of tuberculosis was found on direct smear of the fluid, on cultures, or with guinea pig inoculation. Skin tests with 0.00002 mg. and 0.005 mg. of purified protein derivative were negative. An electrocardiogram was within normal limits.

The patient was given codeine and aspirin for pain and was placed on 100,000 units of crystalline penicillin-G every three hours. He had nausea and emesis during the first 24 hours but thereafter was fairly comfortable. On October 15, 150 c.c. of grossly bloody fluid with a hemoglobin content of 7.5 gm. were removed. An x-ray of the chest on October 18 revealed almost complete reëxpansion of the lung, but there was an increase in the amount of the fluid, with a slight displacement of the mediastinal structures to the right. On that day 1,000 c.c. of bloody fluid were removed. On October 20 an x-ray showed a marked increase in the amount of fluid,



Fig. 3. Chest x-ray, October 25, 1952. Film taken immediately prior to the injection of streptokinase-streptodornase.

with obliteration of the entire left hemithorax and moderate displacement of the mediastinal contents to the right (figure 2). During the next five days further aspirations were done daily, with removal of an additional 4,725 c.c. of bloody fluid, making a total of 5,875 c.c. of fluid removed. The hemoglobin content of the fluid on October 20 was 3.0 gm., and on October 23 it was 1.0 gm. By October 25 it was possible to remove only 275 c.c. of serosanguineous fluid, although an x-ray still showed a considerable amount of fluid remaining at the left base and over the left apex (figure 3). It seemed evident that aspirations alone were not accomplishing a satisfactory result, and it was therefore decided to use streptokinase and streptodornase.

On October 25, 100,000 units of streptokinase and 25,000 units of streptodornase were injected into the pleural space. Within 10 hours the patient's temperature rose to 102° F., his blood pressure dropped to 90/58 mm. of Hg, and he became markedly dyspneic. A thoracentesis removed 1,650 c.c. of serosanguineous fluid and the patient became more comfortable. X-ray showed a marked reduction in the hydrothorax and a return to normal position of the mediastinum. During the next six days an additional 250,000 units of streptodornase were injected into the pleural space in divided doses. Aspirations were

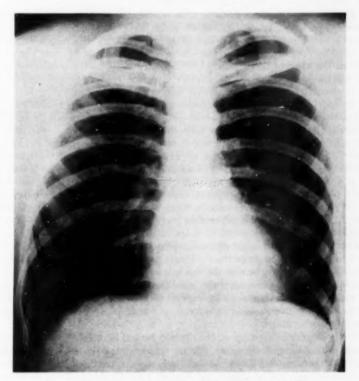


Fig. 4. Chest x-ray, January 20, 1953. Normal chest film.

attempted 24 hours after each injection, but no significant amount of fluid could be withdrawn. With each injection of the enzymes the patient had a febrile reaction, with temperatures ranging to 104.6° F. Serial x-rays of the chest showed gradual diminution of the pleural density, and on November 13 x-ray showed almost complete resolution of the hemothorax. Vital capacity was 100 per cent and the patient was afebrile and asymptomatic. The red blood cell count had risen to 4,100,000 per cubic millimeter, with 12.0 gm. of hemoglobin. The patient was sent home on convalescent leave. A follow-up film on January 20, 1953, was essentially normal in its roentgen appearance (figure 4).

DISCUSSION

Spontaneous hemopneumothorax occurs almost exclusively in young adult males; only four cases in females have been reported.⁴ The average age is between 20 and 40. The reason for this overwhelming sex preponderance is not known. Its allied disorder, spontaneous pneumothorax, occurs almost as frequently in women as in men.

The etiology is usually obscure. However, it is generally felt that the entry of air into the pleural cavity follows the rupture of an emphysematous bleb, and that a tearing of adhesions results, with subsequent bleeding from the parietal surface. The majority of fatal cases which have been examined at autopsy showed apical pleural scars and adhesions. In patients in whom bleeding was controlled by open thoracotomy, the source of bleeding was found in the parietal pleura at the apex of the thorax.^{3, 4, 13} Solovay suggests the possibility that in some instances the condition may result from the rupture of capillaries at the base of alveolar tears occurring during interstitial emphysema.¹⁴

The onset of spontaneous hemopneumothorax may be either insidious, with the gradual development of weakness and chest pain, or it may be acute and dramatically sudden. In the acute form there is usually sudden severe one-sided chest pain, with signs of blood loss and respiratory distress. The pain may be referred to the shoulder or to the upper abdomen. Often the symptoms develop more slowly, with the onset of sudden chest pain followed by a latent period of a few hours or days in which the pain becomes less. This is followed in turn by the gradual development of weakness and dyspnea, and eventual collapse.

The physical findings are usually those of a pneumothorax with pleural effusion. Signs of shock are present in proportion to the amount of blood loss. Mediastinal shift may be noted in cases of massive hemorrhage. The disease often resembles an abdominal catastrophy such as a ruptured viscus, and it also may mimic myocardial infarction. There have been at least two recorded instances of laparotomy before the correct diagnosis was established. A low grade fever usually accompanies this condition, and often there is a leukocytosis. The signs of pneumothorax or hydropneumothorax, however, are usually quite obvious, and the diagnosis is supported by roentgen-ray examination and confirmed by thoracentesis.

The principles of therapy of the chronic hemothorax have undergone major revision during the past six years. In his review of the subject in 1942, Hartzell stated that thoracentesis should be done only for diagnostic purposes and for the correction of mediastinal shift.\(^1\) As late as 1949 Dorset and Terry advocated that a small amount of fluid be aspirated initially for diagnostic purposes, and that only after several days of watching should small amounts of blood be removed every few days, with partial replacement by air.\(^{15}\) The experience gained during World War II has well demonstrated the inadequacy of this conservative management. The incidence of chronic hemothorax and inexpansible lungs is higher in those patients treated by slow aspiration and air replacement than by aspirations done with a view to emptying the pleural cavity and reëxpanding the lung as rapidly as possible.\(^{10}\) Thus, the patient in whom active bleeding has stopped should have his pleural cavity emptied as rapidly as possible by aspirations.

The bleeding soon stops in the majority of the patients. However, there is a considerable percentage in whom the hemorrhage continues uncontrolled. The over-all mortality among cases treated conservatively approaches 25 per cent, and all of the fatal cases reported have died seemingly of massive hemorrhage.^{3, 4} In 1951 Myers reported the first published case of hemopneumothorax treated by open thoracotomy.¹³ Since then there have been at least five additional cases so treated, all with favorable results.^{3, 4, 6} Uncontrolled bleeding into the pleural cavity is a surgical emergency, as is massive hemorrhage occurring in any other part of the body. The individual patient must be closely watched for signs of shock and progressing anemia. In these cases early thoracotomy with direct control of the bleeding is a life-saving procedure.

Once it is clear that the active bleeding has stopped, the problem of preventing a fibrothorax is of immediate concern. Although treatment by aspiration alone often results in complete reexpansion of the lung, many cases have been

reported in which decortication was necessary.

During the past 20 years Tillett and his associates have undertaken a series of laboratory and clinical investigations with two preparations derived from broth cultures of hemolytic streptococci which have been named streptokinase and streptodornase.¹¹ Streptokinase is a catalyst which acts on a fibrolysing system in the blood to produce plasmin, the lytic factor for fibrin and fibrinogen. Streptodornase, or desoxyribonuclease, is an enzyme which causes hydrolysis of desoxyribonucleoprotein and desoxyribonucleic acid. Because of the remarkable ability of these agents to bring about rapidly the liquefaction of human fibrin clots, it was suggested that they might prove useful in treating hemothorax. Three years ago Tillett and Sherry reported the beneficial effects of these enzymes in treating fibrinous, purulent and sanguineous pleural exudations in 23 patients.¹¹ Their use in the treatment of hemothorax has been limited almost exclusively to cases of traumatic or postsurgical hemothorax.^{11, 12, 16, 17} However, Read and Berry reported the successful use of the enzymes in one patient with spontaneous hemopneumothorax.⁸

The use of these agents incites two types of nonspecific reactions. There is a local outpouring of fluid and phagocytes at the site of application, and a pyrogenic reaction occurs, probably due in part to the absorption of the products produced by the enzymes. The temperature ranges up to 105°F. The enzymes should be injected into the pleural cavity early, but only when it is evident that active hemorrhage has ceased. The introduction may be done either by thoracentesis or through a catheter into the pleural cavity. Most authors now are recommending this later method to facilitate drainage. There is usually a dramatic outpouring of fluid, and one must be prepared to remove this fluid within 24 hours, or sooner if there is respiratory embarrassment. Maximal liquefaction usually occurs within 12 to 24 hours, and the enzyme action is completed within 24 to 48 hours. It is suggested that the dose of the initial injection should be 200,000 to 400,000 units of streptokinase and 50,000 to 75,000 units of streptodornase. Although occasionally only one or two injections are necessary in a case of hemothorax, most patients will require more. Treatment with these agents must be individualized, and therapy is guided by temperature curves, the nature of the aspirated fluid and x-rays.

SUMMARY

- 1. A case is reported of spontaneous hemopneumothorax successfully treated with multiple aspirations and the use of streptokinase and streptodornase.
 - 2. The clinical syndrome and the literature are briefly reviewed.
 - 3. A suggested plan of treatment is offered:
 - A. Early and complete removal of both blood and air.
 - B. Early thoracotomy, with direct control of the bleeding if the hemorrhage continues.
 - Adequate supportive measures, including sedation, antibiotics, and blood transfusions if necessary.
 - D. Injection of streptokinase and streptodornase when active bleeding has stopped.

BIBLIOGRAPHY

- Hartzell, H. C.: Spontaneous hemopneumothorax, report of three cases and review of the literature, Ann. Int. Med. 17: 496-510 (Sept.) 1942.
- Eidinger, S. L., and Rubin, E. H.: Spontaneous pneumohaemothorax, report of three cases, Canad. M. A. J. 67: 43–46 (July) 1952.
- Beatty, G. A., and Frelick, R. W.: Hemopneumothorax, reëvaluation of treatment, Ann. Int. Med. 36: 845-851 (Mar.) 1952.
- 4. Ross, C. A.: Spontaneous hemopneumothorax, J. Thoracic Surg. 23: 582-592 (June)
- Cuningham, J. A. K.: Spontaneous haemothorax and haemopneumothorax, New Zealand M. J. 49: 708-712 (Dec.) 1950.
- M. J. 49: 708-712 (Dec.) 1950.
 Holloway, J. B., Speir, R. C., and Sadler, R. N.: Spontaneous hemopneumothorax re-
- quiring thoracotomy, report of a case, Am. Surgeon 18: 518-523 (May) 1952.
 7. Irwin, H. R.: Death due to spontaneous hemopneumothorax, M. Bull. European Command 8: 538-540 (Dec.) 1951.
- Read, C. T., and Berry, F. B.: The utilization of streptokinase-streptodornase in a patient with hemopneumothorax and a patient with postpneumonectomy sanguineous coagulum, J. Thoracic Surg. 20: 384-392 (Sept.) 1950.
- Williams, M. H.: The technique of pulmonary decortication and pleurolysis, J. Thoracic Surg. 20: 652-664 (Oct.) 1950.
- 10. Moore, R. L.: War injuries of the chest, Ann. Surg. 124: 367-382 (Aug.) 1946.
- Tillett, W. S., and Sherry, S.: The effect in patients of streptococcal fibrinolysin (streptokinase) and streptococcal desoxyribonuclease on fibrinous, purulent, and sanguineous pleural exudations, J. Clin. Investigation 28: 173-190 (Jan.) 1949.
- Sherry, S., Tillett, W. S., and Read, C. T.: The use of streptokinase-streptodornase in the treatment of hemothorax, J. Thoracic Surg. 20: 393-417 (Sept.) 1950.
- Myers, R. T., Johnston, F. R., and Bradshaw, H. H.: Spontaneous hemopneumothorax, report of a case treated by thoracotomy, Ann. Surg. 133: 413-416 (Mar.) 1951.
- Solovay, J.: Spontaneous hemopneumothorax, etiological considerations and case report, Radiology 53: 256-260 (Aug.) 1949.
- Dorset, V. J., and Terry, L. L.: Spontaneous hemopneumothorax with recovery, Am. J. Med. 6: 135-138 (Jan.) 1949.
- Miller, J. M., Ginsberg, M., Lipin, R. J., and Long, P. H.: Clinical experience with streptokinase and streptodornase, J. A. M. A. 145: 620-624 (Mar. 3) 1951.
- Miller, J. M., and Long, P. H.: The treatment of hemothorax; with particular reference to the use of streptokinase and streptodornase, U. S. Armed Forces M. J. 3: 1061– 1070 (July) 1952.

ACUTE HEPATITIS DUE TO BRUCELLOSIS*

By H. NUSHAN, M.D., and A. A. BAILEY, M.D., Kecoughtan, Virginia

ACUTE hepatitis due to brucellosis is apparently a rare condition. On reviewing the literature we could find but few references concerning this morbid state. Most authors fail to mention that jaundice may be intense in brucellosis and, if it does occur, they attribute it to some cause other than hepatitis.

Hughes 1 in 1897 stated: "The liver is often tender to pressure and slightly enlarged downward in severe cases at an early stage and also towards the end of prolonged attacks when from continued back pressure it has become somewhat nutmeg in character." Bruce 1 on microscopic examination found cloudy swelling of the liver cells with infiltration of small round cells in the interlobular

Fabyan 2 in 1912, using guinea pigs, the most susceptible small animal in experimental brucellosis, described the pathologic changes that occur. The basic lesion produced was a granuloma, and there was a remarkable similarity to the granuloma observed in tuberculosis. The lesion was more prominent in tissues rich in reticuloendothelial elements. In the guinea pig and the mouse the liver contained more lesions than any other tissue.

Braude and Anderson 2 described the following changes as they occur in the liver and blood stream of the mouse following intra-abdominal inoculation of

brucella:

1. Polymorphonuclear cells with intracellular brucella are found in the circulating blood.

2. Intracellular brucella (polymorphonuclears and Kupffer's cells) are found

in the hepatic sinusoids.

- 3. Focal aggregations of parasitized Kupffer's cells with marked reduction of stray polymorphonuclears are found in the sinusoids.
- 4. The cellular aggregates increase in size to form early granulomas, and there is disappearance of nearly all intracellular organisms.

5. There is fusion of granulomas to form large focal lesions.

- 6. Hyaline degeneration occurs in the centers of the granulomas, and Langhans' giant cells make their appearance.
- 7. The granulomatous reaction then begins to show abatement, and there is reduction in the number of cells surrounding the hyaline center.
- 8. The granuloma disappears without demonstrable scar.

Amoss,3 in reporting on the localization of the brucella organisms, stated that brucella belong to the group of lymphogenic antigens because the defensive factor of phagocytosis by the polymorphonuclear cells is not prominent. He described two patients in whom brucella were recovered from the bile by duodenal drainage. The organism was cultured from the removed thickened gall-bladder. However, there is no mention as to whether either of these patients had jaundice.

From the Veterans Administration Center, Kecoughtan, Virginia.

^{*}Received for publication March 27, 1953. (Read in part before the Regional Meeting of The American College of Physicians, Virginia, at Old Point Comfort, Virginia, February 26, 1953.)

Chaiken and Schwimmer * reported a case of hepatomegaly with jaundice. There was evidence of disturbed liver function as shown by a 4 plus cephalin flocculation, and a total protein of 4.98 with an A/G ratio of 1.0. The icteric index was 16.2. The urine was positive for bile and urobilinogen, while the stools were negative for bile and stercobilin. Eight days after admission to the hospital the patient developed an elevated temperature which persisted for 10 weeks. Blood cultures were negative. Agglutination tests for brucella showed a rising titer up to 1:1280. The icteric index increased to 18. The jaundice disappeared within two weeks of admission, but evidence of liver damage remained for a period of 10 weeks.

Hoffbauer and Spink ⁶ described the findings in liver tissue obtained by biopsy from one patient with acute brucellosis and four with chronic brucellosis. In all specimens granulomata were found in the liver cords. These granulomata consisted of epithelioid cells, lymphocytes and plasma cells arranged in small groups. In addition, the connective tissue in the portal spaces was found to be increased and there was occasional necrosis of liver cells. Multiple liver function tests in

these patients indicated only slight impairment of liver function.

Rossmiller and Ensign a reported a case of jaundice in a white male who had had recurring bouts of fever and chills for four years. Two months before admission to the hospital he developed jaundice, right upper quadrant pain and dark urine. He received streptomycin, and two days before admission there was some diminution in the jaundice. Laboratory examinations revealed an icteric index of 32, a cephalin flocculation of 2 plus and a thymol turbidity of 50 units. The urine was strongly positive for bile and urobilinogen but the stools were normal. Blood culture was positive for Brucella abortus, the agglutination test was positive in a dilution of 1:2560, and the skin test was also positive. The patient was treated with streptomycin and sulfadiazine. The jaundice subsided in a few days, and eight weeks later the liver was no longer palpable or tender.

Harris,⁷ in his book on undulant fever, stated that brucellosis may cause inflammatory changes in the gall-bladder and ducts and that the process may be acute or chronic. He said also that enlargement of the liver with tenderness and dvsfunction is now recognized to be at least as frequent as splenomegaly. Spink and Hall ⁷ observed that it is not unlikely that brucellosis may cause cirrhosis of the liver. Other investigators (Watson, Lowbeer, Zaus and Espey ⁷) are in agreement. Barker, Capps and Allen ⁷ noted a clinical similarity between chronic infectious (virus) hepatitis and hepatitis occurring in chronic brucellosis.

Brucellosis in man is a protean disease (Soule)² in which the state of nutrition is of major importance. In general the prognosis is good, for the disease is self-limited and complete recovery may follow from mere bed-rest. For nearly 50 years various antigens were introduced into the body by every possible route with unsatisfactory therapeutic results. Nonspecific protein shock and hyperthermy were not too helpful. Sulfonamides did not prove as successful as was first thought. Combined therapy with streptomycin and sulfadiazine has shown real promise, but relapses do occur. Aureomycin and chloramphenicol therapy in recent years has given uniformly good results.

Young " reported the case of a colored female who had hepatomegaly, ascites and splenomegaly. Liver function studies revealed hepatocellular damage. No mention was made of jaundice. Blood culture was negative but the agglutination

test was positive in high titer, as was the skin test. A positive culture, Br. abortus, was obtained from a subcutaneous accumulation of fluid from the inguinal region where a lymph node had been excised. A liver biopsy revealed findings which were nonspecific and could be interpreted as an early Laennec's cirrhosis. The patient was treated with sulfadiazine, with improvement in the clinical symptoms.

Pottenger of treated four patients in whom brucellosis was suspected with a mineral salt mixture containing cobalt, manganese, copper and iodine. His results were encouraging. The rationale for this therapy was the fact that manganese, among other substances, was able to counteract the SS (smooth selecting) factor of normal human, boying or guinea pig serum in vitro.

Gigante 10 reported a case of brucellosis complicated by cirrhosis of the liver

with jaundice and ascites which was cured by aureomycin.

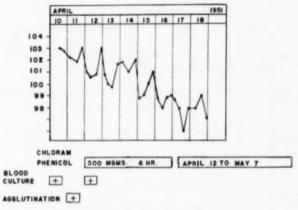


Fig. 1. Temperature chart.

Figuera de Benito,¹¹ in a series of 30 cases of brucellosis studied from a hepatic viewpoint found evidence of hepatic involvement in 19. He stated that usually there is no clinical icterus. He has used combined therapy with good results. Only a few cases were treated with aureomycin or chloramphenicol, but relapses did occur.

CASE REPORT

A 37 year old Negro male slaughter-house worker (who handled hogs almost exclusively) was admitted to the hospital on April 10, 1951, with a chief complaint of weakness. Two weeks before admission he had begun to have chills, fever and sweating. The chills recurred about once or twice a week but the fever was quite constant. Profuse sweats had occurred frequently. At the onset he had pain in the cervical and thoracic spine but this disappeared after a week. His appetite had been poor and he had vomited white material once or twice. "Light pains" had been noticed in the lower abdomen at times. During the week prior to admission he had two loose yellow stools daily. He had severe headaches and vertigo prior to the onset. His eyes had been yellow for about a week. There was no history of hypo-

dermic or intravenous injections or of the withdrawal of blood. He had served in the U. S. Army from 1944 to 1946 but had had no foreign duty. The past history was essentially negative.

Physical examination revealed a Negro male who showed pallor, weakness, emaciation, marked prostration and sweating. Temperature was 103° F.; pulse, 104; respirations, 24; blood pressure, 104/78 mm. of Hg. The sclerae were yellow. Soft systolic murmurs were heard at the base and the apex of the heart. The abdomen was normal; the liver and spleen were not palpable. The posterior cervical, axillary and inguinal lymph nodes were palpable. The temperature chart is pictured in figure 1 and the laboratory determinations in table 1. The patient was placed on a

TABLE I

	April 11	April 12	April 13	April 18	April 30	May 2	May 4	May 9	May 29	June 4	June 5	June 26	July 11
Icteric Index	80			23	24	21		15	11		22	8	8
Blood: White blood cells Polymorpho- nuclear Hemoglobin	11,500 74 10.8		4600 26 8.6		6300 24 10.4	4700 28 11.4	4700 25	5700 21 13	7850 42 14.5	4250 39 14.5		6350 61 16.7	4400 34 13.4
Urine	Bile + Albumin & Casts	Bile + Urobil- inogen 1:128	No Albumin or Casts		Neg.	Neg.							
Cephalin flocculation			4+	-	3+			3+	2+		2+	3+	1+
Total protein						3.6		4.5	6.3			6.0	5.7
A/G ratio						1.0		1.1	1.3			1.0	1.1
Nonprotein nitrogen			45	20									
Blood culture for Br. suis	+		+										
Agglutination for Br. abortus		1:20,480											
Agglutination of own organisms against his serum						1:327,000							

Examination of blood for sickling: negative. Agglutinations to typhoid and proteus OX-19: negative. Kahn: negative. Blood sugar: 89 and 106 on two tests. Darkfield examination of blood for leptospira: negative. Guinea pig inoculation with blood for leptospira: negative.

Two positive blood cultures were obtained; in each the organism was identified as Brucella

Note: The Army Medical Center confirmed identification of the organisms in the culture as Br. suis.

high protein, high carbohydrate diet, and on the second day received 2,000 c.c. of 5 per cent dextrose in water intravenously. Chloramphenicol, 500 mg. every six hours, was started on the third hospital day and was continued until May 7. X-ray of the chest was essentially negative, and a flat film of the abdomen revealed no hepatic or splenic enlargement. The patient began to feel better the day after the antibiotic was started but had some upper left quadrant pain for several days. His temperature became normal four days after the chloramphenicol was started. He was allowed out of bed on April 27 and was discharged from the hospital on July 12, after several trial periods at home. He reported back on February 18, 1953. He stated that he had been well since discharge from the hospital and had worked steadily. No further

hospitalization had been required and he had seen a physician only once, about five months previously, for an upper respiratory infection. Urinalysis was normal. Blood studies showed the following: white blood cells, 6.800, with 69 per cent polymorphonuclears; hemoglobin, 9.8 gm.; hematocrit, 38; total protein, 5.7 gm. per cent, and A/G, 1.1. The icteric index was 7 and the cephalin flocculation 3 plus. Agglutination to Br. abortus was positive in a dilution of 1:80.

Brucellosis in man today is, with few exceptions, a sporadic occurrence and not many cases are reported from a rural county during the course of an entire year (Jordan).² Infectious hepatitis may also occur in sporadic fashion. Jaundice and liver dysfunction can occur in both diseases. It is quite important that the differential diagnosis be made, because adequate treatment of brucellosis could prevent a long period of invalidism. The diagnosis can be made only by laboratory means, blood culture and serial agglutination tests.

SUMMARY

- 1. The pathologic changes that occur in the liver in brucellosis were reviewed.
- 2. A case of brucellosis due to Br. suis was presented. The patient showed marked jaundice and abnormal liver function tests, although there was no enlargement of the liver.
- 3. Chloramphenicol therapy produced very rapid and marked clinical improvement. Liver function tests showed some abnormalities for more than 10 weeks
- 4. It is important to consider hepatitis due to brucellosis in the differential diagnosis of hepatitis.

BIBLIOGRAPHY

- Hughes, M. L.: Mediterranean, Malta or undulant fever, 1897, Macmillan and Co., Limited, London, England.
- Brucellosis: A symposium under the joint auspices of National Institutes of Health
 of the Public Health Service, Federal Security Agency, U. S. Department of Agriculture National Research Council, a publication of the American Association for the
 Advancement of Science (Sept. 22, 1923), 1949, Waverly Press, Inc., Baltimore.
- 3. Amoss, H. L.: Localization of brucella, Internat. Clin. 4: 93-98 (Dec.) 1931.
- Chaiken, N. W., and Schwimmer, D.: Hepatitis in the course of brucella infection, Rev. Gastroenterol. 10: 130-132 (Mar.-Apr.) 1943.
- Hoffbauer, F. W., and Spink, W. W.: Biopsy of liver in patients with active brucellosis; description of hepatic lesions, J. Lab. and Clin. Med. 32: 315-316 (Mar.) 1947.
- Rossmiller, H. R., and Ensign, W. G.: Hepatitis associated with undulant fever, Cleveland Clin. Quart. 15: 184-185 (Oct.) 1948.
- 7. Harris, H. J.: Brucellosis (undulant fever), 1950, Paul B. Hoeber, Inc., New York.
- Young, J. D.: Brucellosis with hepatomegaly and splenomegaly, Memphis M. J. 22: 168-170 (Oct.) 1947.
- Pottenger, F. M., Jr.: The use of copper, cobalt, manganese and iodine in the treatment of undulant fever, Ann. West. Med. and Surg. 3: 309-313 (Sept.) 1949.
- Gigante, D.: Un caso di infezione brucellare con epatite itterigena ed ascitogena guarita con aureomicina, Acta med. ital. 6: 70-72 (Mar.) 1951.
- Figuera de Benito, E. de la: Sobre las hepatitis melitococicas anictericas, Rev. españ. enferm. ap. digest. y nutrición 10: 229-236 (May-June) 1951.

SICKLE CELL ANEMIA TERMINATING IN ACUTE MYELOBLASTIC LEUKEMIA*

By Albert G. Goldin, M.D., Karl C. Kelty, M.D., and Marion F. Beard, M.D., F.A.C.P., Louisville, Kentucky

SINCE Herrick's description of sickle cell anemia in 1910 ¹ the literature on this disease has been abundant, with the result that its natural course is fairly well documented. Termination ordinarily occurs before middle age, death usually resulting from intercurrent infections, sickle cell crises, cardiac failure, or hemorrhage or infarction of the brain, as well as from transfusion reactions incident to therapy.^{2, 3}

The finding of leukemoid reaction is not uncommon in various hemolytic anemias, 4, 5 including sickle cell anemia. The difficulty in differentiating some leukemoid reactions from acute leukemia has been pointed out by nearly all writers on the subject.

The following case is deemed worthy of reporting first, because it emphasizes the problem of differentiating leukemia from leukemoid reaction, and second, because we believe it represents a case of sickle cell anemia terminating in acute myeloblastic leukemia, a situation not previously reported, to our knowledge.

CASE REPORT

Present Illness: A 38 year old Negro male was admitted to the medical service on June 11, 1951, acutely ill. He gave a history of onset of sore throat two weeks prior to admission, associated with feverishness and chilly sensations. The throat was so sore that in the week prior to admission he had been unable to swallow anything but liquids, and those with great difficulty. He felt very weak and had lost 12 pounds in the preceding two weeks. Four days before admission he had been seen in the Out-Patient Clinic with the same complaints and was given daily penicillin injections. With failure to respond, he was admitted to the ward.

Physical Examination on admission revealed an acutely ill colored male with the following significant findings: temperature, 103° F.; pulse, 110/min.; respirations, 36/min. The sclerae showed a questionable icteric tinge. A tender node, 2 by 4 cm., was palpated in the right submandibular region, and a few shotty nodes were scattered along the anterior cervical region. No other lymph nodes were felt. The neck was sore to palpation. The throat was very red, with a dirty gray membrane over the tonsils and posterior pharyngeal wall. The lungs were normal. The heart was moderately enlarged to the left, and a systolic grade II murmur was heard over the entire precordium. Blood pressure was 110/40 mm. of Hg. The liver margin was felt 4 cm. below the right costal margin; it was firm and very slightly tender. The spleen was not palpable.

Past History: The patient had had 10 previous admissions to this hospital, seven of them since November, 1948. All of these admissions except one were for complications of sickle cell anemia. These will be briefly abstracted.

The first admission, in February, 1942, was for treatment of a chronic ulcer of the left ankle (medial malleolus), which he stated had been present intermittently

*Received for publication April 15, 1953.

From the Department of Medicine and Division of Hematology, Louisville General Hospital, Louisville, Kentucky.

since the age of 15. It had recently been causing pain on walking. A saphenous ligation two months previously had not caused improvement. Pertinent physical findings, in addition to the ulcer, were a loud systolic apical murmur, and a liver palpable two fingerbreadths below the right costal margin. A 4 by 4 cm. ulcer was present over the left medial malleolus.

The blood count showed 2.5 million erythrocytes/cu. mm., 7.0 gm. of hemoglobin/100 c.c., 13,900 leukocytes/cu. mm., with a normal differential count. The sedimentation rate was 14 mm./hr. Blood transfusions and local treatment to the ulcer resulted in improvement.

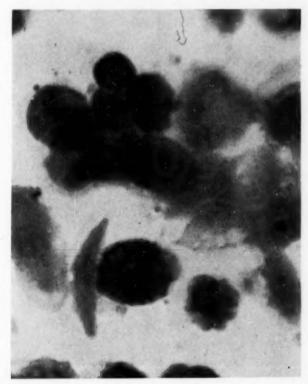


Fig. 1. Bone marrow aspiration, January 14, 1950. (×1350) Normal bone marrow constituents are seen.

In June, 1942, the patient was admitted to the ward for a second time with chickenpox. He had 1.8 million erythrocytes/cu. mm., and 7.5 gm. of hemoglobin/100 c.c. The leukocyte count was 9,900/cu. mm. Many sickled cells were seen in the counting chamber.

The third admission was in September, 1942. Predominant symptoms were weakness and lightheadedness for one week. Physical examination again revealed a systolic apical murmur, slight left ventricular enlargement, moderate liver enlarge-

ment and ulcerations of the left ankle. The erythrocyte count was 2.77 million/cu. mm., with 6.5 gm. of hemoglobin/100 c.c. Numerous sickle cells were noted on special slide preparations. A bone marrow aspiration showed only moderate erythrocytic hyperplasia. Blood transfusions were again administered, and after discharge the leg ulcers gradually healed; after about a year they reappeared, but were cared for by the patient himself and he was not seen again until 1948.

In November, 1948, he was admitted to the hospital for the fourth time, complaining of intermittent sharp shooting pains along the left side of the body of about

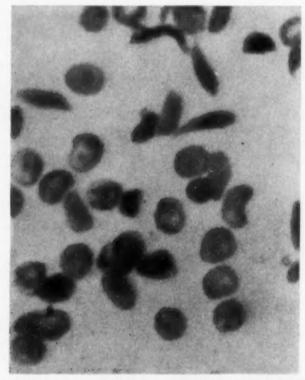


Fig. 2. Peripheral blood, June 12, 1951. (×150) Myeloblasts and sickled cells are seen in the peripheral blood.

three months' duration. He had also been having exertional dyspnea and palpitations for one month. The physical examination was as before except that the leg ulcer was healed. The erythrocyte count was 1.92 million/cu. mm., with 7 gm. of hemoglobin/100 c.c. Sixty per cent sickling of the red blood cells was noted in 72 hours. The total leukocyte count was 14,450/cu. mm., with a differential count of 54 per cent neutrophils, 16 per cent lymphocytes, 22 per cent monocytes, 3 per cent eosinophils and 5 per cent basophils. The serum bilirubin was estimated at 4.1 mg. per cent. The cephalin flocculation test was 3 plus. The patient received 2,000 c.c. of whole

blood in a period of one week, with febrile reactions on several occasions. Afterwards, he had 9 gm. of hemoglobin/100 c.c. and 3.49 million red blood cells/cu. mm. He felt considerably better and after discharge was not seen again for six months.

In May, 1949, he returned for his fifth admission to the hospital with symptoms of weakness, easy fatigability, frontal headache, and "aches and pains all over the body," especially in all the joints. These were of two weeks' duration.

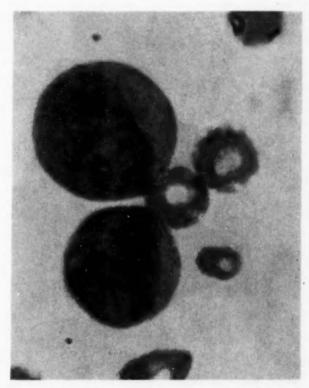


Fig. 3. Bone marrow aspiration, June 13, 1951. (×1350) Typical cell which predominated in the bone marrow is shown. Note several nucleoli.

Marked pallor of the mucous membranes was present, in addition to the physical findings previously noted. A small ulceration was again present over the left medial malleolus. At this time he had 1.03 million red blood cells/cu. mm., with 3 gm. of hemoglobin/100 c.c. There was extensive sickling of the red blood cells. The leukocyte count was 11,800/cu. mm. After transfusions amounting to nine pints of whole blood his hemoglobin rose to 13.5 gm./100 c.c. and the erythrocyte count was 4.31 million/cu. mm. The leukocyte count was 8,100/cu. mm.

In January, 1950, he was hospitalized for the sixth time. Shortness of breath and weakness were again his chief complaints. These had been present for three

weeks. The physical examination was again essentially unchanged except that the

The laboratory examinations revealed the following: red blood count, 1.90 million/cu. mm.; hemoglobin, 7.0 gm./100 c.c.; white blood count, 8,300/cu. mm., with 75 per cent neutrophils, 24 per cent lymphocytes, 1 per cent monocytes. There were 20 per cent reticulocytes. Hematocrit was 20 per cent; MCV, 105.2; MCH, 37.8; MCHC, 36.

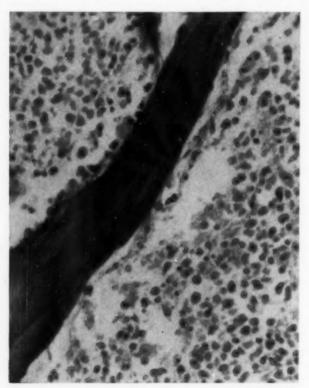


Fig. 4. Bone marrow section from autopsy, June 19, 1951. (×645) Increased cellularity of the marrow and abnormal elements are seen.

Complete sickling of the red cells occurred in two hours. The sedimentation rate in one hour was 5 mm. Serum bilirubin was 3.67 mg. per cent. Cephalin floculation was 2 plus. A bone marrow study showed a marked stimulation of the erythrocytic series. The megakaryocytic series was relatively depressed, but a few young forms were seen. The granulocytic series was relatively depressed. Phagocytosis was not increased. With blood transfusions the patient improved and was discharged.

In June, 1950, he was put to bed with thrombophlebitis involving vessels of the left thigh and calf and left antecubital space. At this time a chest plate showed fine nodular markings throughout both lung fields. An electrocardiogram showed mini-

mal changes in RS-T segment and T wave contour. Again severe anemia was present, this time the red cell count being 760,000/cu. mm. As before, multiple blood transfusions resulted in improvement and, in addition, a lumbar sympathetic block was done with relief of calf and thigh pain.

Another admission was made in August, 1950, for severe anemia, weakness and pain in the precordium not related to exertion. Transfusions were again given,

with improvement.

The ninth and tenth admissions were in December, 1950, and March, 1951, with weakness, chest pain and, this time, slight swelling of the legs. In addition to the physical findings noted previously, a 1 plus pitting edema of the ankles was present. Again, blood transfusions resulted in relief. Records of blood counts during the last two admissions were lost.

Laboratory Findings: On admission a complete blood study was done. The leukocyte count was 157,000/cu. mm. Red blood cells were 1.4 million/cu. mm., hemoglobin was 3.6 gm./100 c.c., and hematocrit was 13.5. The platelets numbered 7,000/cu. mm. by the method of Dameshek. There was 0.1 per cent reticulocytes. Mean cell volume was 96.5 and MCHC was 26.7. The differential count of the leukocytes showed 20 myelocytes, 75 myeloblasts, 4 basophils and 1 lymphocyte. A

TABLE I
Results of Peripheral Blood Counts during Last Hospitalization

	R.B.C.					Differential		
Date	Million	W.B.C.	Hgb.	Platelets	Retic.	Total Lymphoid	Total Myeloid	
6-11	1.74	166,000	4.5					
6-12	1.4	157,000	3.6	7,000	0.1%	1	99	
6-13	2.0	143,000	4.7	12,000	0	0	100	
6-14	2.0	75,000	4.9	6,000	0.1%	0	100	
6-15	2.1	38,000	5.9	6,300	0.1%	0	100	
6-16	2.20	37,500	5.5	11,000	0.1%	1 1	99	
6-18	1.50	500	5.2	_	0	0	100	

bone marrow aspiration was done, the specimen having been taken from the right ilium. Grossly it was of normal appearance, but microscopically there were only myeloblasts and early myelocytes, to the exclusion of all other cells. The impression was acute myeloblastic leukemia.

Hospital Course: The temperature spiked several times daily to heights of 105° F., continuing in this manner until death, despite antipyretic measures including salicylate and alcohol sponges. Oral and parenteral fluids were given in addition to frequent small transfusions of whole blood totaling 2,500 c.c. Penicillin and streptomycin were also administered during the course of the illness. On June 13, 1951, the white count was 143,000/cu. mm., with 85 per cent myeloblasts, 13 per cent early myelocytes and 2 per cent basophils. The platelet count was 12,000/cu. mm.

A-methopterin, 2.5 mg. every 24 hours, was started on June 13, 1951 and continued through June 18. On June 14 a watery diarrhea developed and became more severe, though not bloody, during the hospital course. The patient became stuporous on June 18 and died the next day. Almost daily blood counts were taken and are listed in table 1.

AUTOPSY FINDINGS

Grossly the head was normal. Permission was not given for examination of the cranial cavity. The epiglottis, larynx and trachea appeared normal. Thorax:

The right lung weighed 630 gm. and the left lung, 420 gm. There was excessive hemorrhagic fluid throughout. There were scattered firm, dark areas which were microscopically identified as focal fresh hemorrhages. There was no leukemic infiltration. The heart weighed 370 gm. The myocardium, endocardium and vessels appeared normal grossly, as did the valves. Microscopically a well marked "brown atrophy" was noted. There was no leukemic infiltration. The remaining mediastinal structures were normal grossly, except the esophagus, which showed extensive shallow ulcerations of the type seen with anti-folic acid therapy. Abdomen: The liver weighed 2,460 gm, and grossly showed no abnormality. Histologically there was extensive hemosiderosis, with the pigment largely in the Kupffer cells. The spleen was extremely shrunken, measuring 4 by 2 by 2 cm, and weighing 5 gm. The cut surface was light gray and firm, except for one small area of reddening. Histologically it showed extensive fibrous atrophy and hemosiderosis. There was no leukemic infiltrate. The pancreas weighed 130 gm. and appeared edematous. There were several enlarged lymph nodes along its superior border. Microscopically there was only mild hemosiderin deposition. Multiple sections of lymph nodes failed to reveal any evidence of leukemic infiltration. There was moderate hemosiderin deposition and reticulum cell hyperplasia in the lymph nodes. The kidneys weighed 230 gm. each. The cut surfaces appeared normal and capsules stripped easily. Histologically there was minimal hemosiderin deposition in the tubules. There were no leukemic infiltrations.

The remaining abdominal contents were normal. The bone marrow exhibited an almost complete replacement by blast cells. Only an occasional erythroblast or normoblast was seen, and no megakaryocytes were noted. In the blood vessels of numerous tissues sickled red cells could be seen.

The final pathologic diagnosis was: (1) blast cell leukemia; (2) sickle cell anemia; (3) hemosiderosis of liver, spleen and kidneys; (4) pulmonary edema and hemorrhage; (5) ulcerations of the esophagus, probably secondary to therapy; (6) fibrous atrophy of spleen.

COMMENT

The obvious difficulty in the evaluation of this patient's condition lies in distinguishing a leukemia from a leukemoid reaction. This differentiation ordinarily presents little difficulty when one has the opportunity to follow the clinical course, and to make repeated studies of the peripheral blood and bone marrow. However, there are instances in which the differentiation of the two conditions may not be possible during life or even at autopsy.⁷

The peripheral blood examination in this case was obviously compatible with leukemia, showing as it did an elevation of the leukocyte count with an over-whelming predominance of myeloblasts and myelocytes. On the other hand, if it were the only factor to be considered, it would fall into the category of leukemoid reaction, with only a hematologic similarity to leukemia, as described by Krumbhaar.⁷

Wintrobe states that a low platelet count is an almost invariable accompaniment of acute leukemia and that leukemoid reactions are unlikely to be accompanied by a thrombocytopenia. Several platelet counts in this study did not exceed 12,000/cu. mm., even before A-methopterin therapy was started. This factor lends further support to the diagnosis of leukemia.

In earlier reports of the leukemoid reaction 4. 5, 7, 8 the bone marrow examinations are not described. More recently, examination of the bone marrow during life has become widespread, and apparently is of considerable aid in differentiating the two processes under discussion. In acute myeloid forms of leukemia, the bone marrow is usually predominated by myeloblasts and other primitive forms of the myeloid series. However, the leukemoid bone marrow ^{9, 10} usually shows a nonspecific type of hyperplasia in which the precursors of the granulocytes are not particularly prominent. The bone marrow in this case showed only myeloblasts and very early myelocytes to the exclusion of all other cells.

This further supports the diagnosis of leukemia.

The clinical picture should be of considerable aid in establishing the diagnosis. Here, a typical onset of acute leukemia with a severe necrotizing pharyngitis and fever of a "septic" type is present. A clinical hemorrhagic tendency, so common in the acute leukemia, was inexplicably not present in this patient, despite the low platelet count. However, at autopsy pulmonary hemorrhages were noted, possibly on the basis of decreased platelets. The lymph nodes were not enlarged except in the cervical region, where the pharyngitis might easily account for it. In acute myeloblastic leukemia, however, lymphadenopathy may be insignificant or absent. An enlarged spleen is ordinarily present in leukemia, but it is not always palpable. Here the fibrous atrophy of the spleen associated with the sickle cell anemia obviously precluded its enlargement in the leukemic process.

The patient's rapid downward course terminating in death favors leukemia, though a terminal leukemoid reaction in a severe sickle cell crisis must also be considered. This would place this case in the category of one manifesting real difficulty in differentiation from leukemia, as described by Krumbhaar.

The very severe anemia on admission is difficult to evaluate. It could represent the anemia of leukemia superimposed on the chronic sickle cell anemia, but it could also have resulted from a severe hemolytic crisis upon which a leukemoid reaction was ingrafted. Unfortunately, studies adequate to elucidate this point were not done.

The autopsy findings remain to be discussed. The absence of leukemic infiltration in any of the viscera or nodes is somewhat disturbing and may detract from the conclusiveness of the diagnosis. However, in a fulminating acute leukemia such as this, there may not have been enough time to develop infiltrations. Furthermore, the administration of A-methopterin may have suppressed or "melted" leukemic foci in the tissues, as it did in the peripheral blood count. This is conjectural, and it should be noted that despite the treatment the bone marrow at autopsy still showed an almost complete replacement by blast cells.

In our opinion, the evidence thus considered leads to the diagnosis of acute myeloblastic leukemia.

A review of the literature available to us has failed to reveal a reported case of the coexistence of sickle cell anemia and leukemia. Kato and Cardozo 11 reported a case of coexistence of sicklemia and Hodgkin's disease. They felt, as do we, that the combination is fortuitous and, on this basis, unusual. No relationship, etiologically, is felt to exist between the two diseases.

SUMMARY

 A case of sickle cell anemia terminating in acute myeloblastic leukemia is presented.

2. The differentiation of leukemia from leukemoid reaction is discussed.

BIBLIOGRAPHY

- Herrick, J. B.: Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia, Arch. Int. Med. 6: 517-521, 1910.
- Graham, G. S., and McCarty, S. H.: Sickle cell (meniscocytic) anemia, South. M. J. 23: 598-607, 1930.
- Henderson, A. B.: Sickle cell anemia, clinical study of fifty-four cases, Am. J. Med. 9: 757-765, 1950.
- Heck, F. J., and Hall, B. E.: Leukemoid reactions of the myeloid type, J. A. M. A. 112: 95-101, 1939.
- 5. Hill, J. M., and Duncan, C. N.: Leukemoid reactions, Am. J. M. Sc. 201: 847-857, 1941.
- Wintrobe, M. M.: Clinical hematology, 3rd Ed., 1951, Lea & Febiger, Philadelphia, pp. 853-854.
- 6. (a) Ibid: p. 834.
- Krumbhaar, E. B.: Leukemoid blood pictures in various clinical conditions, Am. J. M. Sc. 172: 519-533, 1926.
- Downey, H., Major, S. G., and Noble, J. F.: Leukemoid blood pictures of the myeloid type, Folia haemat. 41: 493-511, 1930.
- Leitner, S. J.: Bone marrow biopsy. Hematology in the light of sternal puncture, 1949, Grune & Stratton, New York, pp. 234-243.
- Custer, R. P.: An atlas of the blood and bone marrow, 1949, W. B. Saunders Co., Philadelphia, pp. 188-197.
- Kato, K., and Cardozo, W. W.: Hodgkin's disease with terminal eosinophilia occurring in a Negro child with sicklemia, J. Pediat. 12: 165-175, 1938.

AN UNUSUAL CASE OF MASSIVE PERICARDIAL EFFUSION WITH HEMODYNAMIC STUDIES*

By Paul N. G. Yu, M.D., Frank W. Lovejoy, Jr., M.D., Howard A. Joos, M.D., Robert E. Nye, Jr., M.D., Rochester, N. Y., and John H. Simpson, M.D., M.R.C.P., Norwich, England

Despite clinical and pathologic investigations of many patients with pericardial effusion, 1-6 few such patients have been studied by cardiac catheterization. 6, 7 It is the purpose of this manuscript to present clinical and hemodynamic observations on a patient with massive pericardial effusion. Cardiac output, intravascular and intrapericardial pressures, blood gas analysis and other related clinical and laboratory findings are described before and after pericardial aspirations and six months following pericardiectomy.

CASE REPORT

A 70 year old tailor was hospitalized on February 29, 1952, with a history of repeated attacks of acute dyspnea for about 18 months. For one year prior to ad-

* Received for publication June 5, 1953.

From the Chest Laboratory of the Department of Medicine of the University of Rochester School of Medicine and Dentistry, and the Medical Clinics of Strong Memorial and Rochester Municipal Hospitals. Rochester, New York.

and Rochester Municipal Hospitals, Rochester, New York.

This study was supported in part by a research grant-in-aid from the National Heart Institute of the National Institutes of Health, Public Health Service, The Hochstetter Fund, and Ernest L. Woodward Fund.

mission he had also noticed increasing exertional dyspnea, frequent palpitation and the loss of about 15 pounds in weight. Six months prior to admission he first noticed swelling of the ankles.

In November, 1950, he was seen in another hospital. At that time the pertinent physical and laboratory findings included the following: (a) distended jugular veins and enlarged liver; (b) bilateral cardiac enlargement with inaudible heart sounds

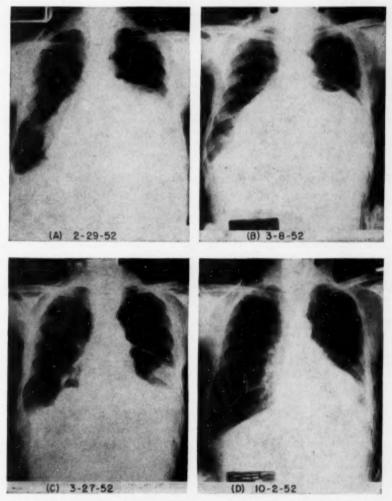


Fig. 1. Representative serial roentgenograms of the chest are shown. (A) On admission; (B) After removal of 1,400 c.c. of pericardial fluid and injection of 200 c.c. of air; (C) Suspected tumor in the right lower portion of the pericardium; and (D) Six months following pericardiectomy. Note adhesion along the left border of the heart.

at the apex; (c) marked enlargement of the cardiac shadow with no discernible pulsation by fluoroscopic examination; (d) extremely low voltage of the QRS complex of the electrocardiogram in all limb and precordial leads; and (e) delayed arm-to-tongue circulation time (29 seconds). The provisional diagnosis was pericardial effusion. The patient discharged himself against advice before further studies were conducted.

At the time of admission to this hospital the patient's temperature was 37.5° C.; respirations, 20; pulse rate, 92; blood pressure, 124/80 mm. of Hg. The normal pulse pressure is noteworthy. He appeared chronically ill and orthopneic. The jugular veins were distended and pitting edema of both legs was pronounced. The lungs were clear except for a few moist râles over the base of the left lung. The area of cardiac dullness was markedly enlarged bilaterally and the heart sounds were inaudible. The liver edge was palpable 4 to 5 cm. below the costal margin.

The admission white blood count was 4,500 per cubic millimeter, with 73 per cent polymorphonuclear cells, 19 per cent lymphocytes, 7 per cent monocytes and 1 per cent basophils. Hemoglobin was 12.8 gm. per cent and hematocrit 40. Vital capacity was 1,200 c.c., and circulation time arm-to-tongue (Decholin), 30 seconds. The venous pressure was 22 cm. of saline (16 mm. Hg). Blood urea nitrogen, chloride, sodium, potassium and CO₂ combining power were all normal. A 12-lead electrocardiogram showed very low voltage and flat or slightly inverted T waves in all limb and precordial leads. A mini-chest x-ray (figure 1A) showed a large globular cardiac shadow occupying most of the left and the lower half of the right lung field. The admission diagnosis was massive pericardial effusion of unknown etiology.

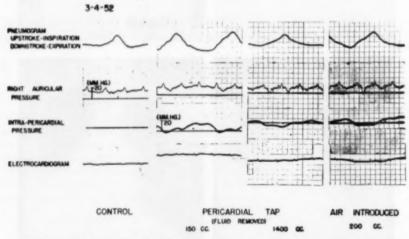


Fig. 2. Pressure tracings obtained in the right atrium and pericardial cavity during the first pericardial aspiration on March 4, 1952. Before aspiration the right atrial pressure was markedly elevated with little respiratory effect, and no M or W shaped pattern. After 150 c.c. of pericardial fluid had been withdrawn the right atrial pressure declined during inspiration. This effect increased after 1,400 c.c. of fluid had been removed. Although the right atrial-intrapericardial mean pressure gradient was always above 10 mm. Hg, the gradient during the expiratory pause was narrow (see figure 3). The mean intrapericardial pressure was positive after withdrawal of 150 c.c. of fluid, but became negative after the removal of 1,400 c.c. After 200 c.c. of air had been introduced into the pericardial sac both the right atrial and intrapericardial mean pressures rose.

Fluoroscopic examination on March 3 showed no visible pulsation of the heart. With barium swallow there was generalized posterior displacement of the esophagus. A small amount of fluid was present in the right costophrenic angle.

The first cardiac catheterization and pericardial aspiration were performed on March 4. Due to technical difficulty the catheter could not be advanced beyond the right atrium. With the tip of the catheter in the right atrium, the pericardium was tapped through the left costoxiphoid angle. As fluid was withdrawn the right atrial and intrapericardial pressures were recorded simultaneously at frequent intervals (figure 2).* Fourteen hundred cubic centimeters of fluid were aspirated and 200 c.c. of air introduced to demonstrate by x-ray the size of the pericardial sac.

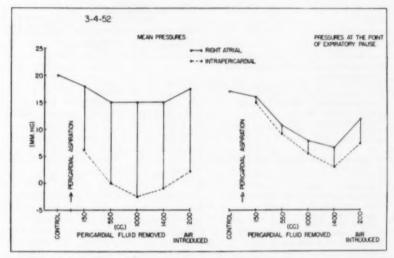


Fig. 3. On the left the simultaneous mean right atrial and intrapericardial pressures are shown during the first pericardial aspiration on March 4, 1952. Note the wide gradient between the mean pressures in these two chambers and also the negative mean intrapericardial pressure after more than 1,000 c.c. of pericardial fluid had been withdrawn. On the right the simultaneous right atrial and intrapericardial pressures measured at the point of expiratory pause are shown. Note the narrow pressure gradient in the beginning which became considerably widened after the removal of 1,400 c.c. of pericardial fluid.

The fluid removed was dark yellow-brown and turbid, and contained a moderate amount of fibrin. The total cell count was 27,000 per cubic millimeter, 6,900 of which were white blood cells, predominantly lymphocytes. There were many small, sheetlike crystals resembling cholesterol. No bacteria were seen on smears stained with gram and Ziehl-Neelsen stains. Anaerobic and aerobic cultures were sterile. Guinea pigs inoculated with pericardial fluid did not acquire tuberculosis. Cytologic and pathologic examination revealed no malignant cells. The total protein of the fluid measured 6.05 gm. per cent, and the cholesterol, 12 mg. per cent.

After pericardial aspiration the patient felt much more comfortable. The venous pressure was reduced to 18 cm. of saline (13 mm. Hg). Figure 1B shows a PA chest

^{*}With the patient in a semi-sitting position, the zero reference level for atrial and intrapericardial pressures was essentially the same, the difference being estimated as less than 1.0 mm. Hg.

film taken on March 8. Fluoroscopic examination on the same day showed the pericardial sac grossly distended by free fluid and some air. With each heart beat a definite undulation of the fluid was seen. The configuration of the heart appeared to be normal.

The next day the patient developed intermittent fever which persisted for the following five weeks. On March 9 a pericardial friction rub was heard which dis-

TABLE I

Hemodynamic Studies and Blood Gas Analysis before and Immediately after the Second
Pericardial Aspiration and Six Months after Pericardiectomy

	I. (3/12/52) Second Pericardial Aspiration		II. (10/18/52) Six Months After
	Before	Immediately After	Pericardiectomy
A. Determination of Cardiac Output and Stroke Volume Oxygen consumption (c.c./min./M2, BSA) A-V O ₂ difference (vol. %) Cardiac index (L./min./M2, BSA) Cardiac output (L./min.) Heart rate (beats/minute) Stroke index (c.c./min./M2, BSA) Stroke volume (c.c./min.)	176 6.4 2.75 4.32 92 30 47	160 6.2 2.58 4.05 83 31 49	157 6.2 2.53 4.12 70 36 59
B. Measurement of Pressures and Resistance (1) Pressures in mm. Hg Brachial artery (S/D, mean) "Pulmonary capillary" (mean) Pulmonary artery (S/D, mean) Right ventricle (S/D, mean) Right atrium (mean) Superior vena cava (mean) (2) Resistance in dynes-seccm.—4 Total peripheral resistance Total pulmonary resistance Pulmonary arteriolar resistance	124/80* 12 16 	8 10	161/83, 110 22 47/20, 27 45/5 6 2140 524 97
C. Blood Gas Analysis (1) Arterial blood Pacos (mm. Hg) Paos (mm. Hg) COs content (vol. %) Os capacity (vol. %) Os saturation (%) (2) Mixed venous blood COs content (vol. %) Os saturation (%)	47 68 49.1 14.1 15.6 90.4 53.5 7.7 49.6	41 71 49.2 14.4 15.6 92.2 53.4 8.2 52.7	40 79 50.7 17.6 18.7 94.1 53.6 11.4 60.9

^{*} Measured by sphygmomanometry.

appeared about eight hours later. An intradermal test with old tuberculin in 1:1,000 dilution was negative after 48 hours. During this week four blood cultures and one bone marrow culture were made and remained sterile after two weeks' incubation. On March 12, cardiac catheterization and pericardial aspiration were repeated. Again it was not possible to advance the catheter beyond the right auricle. The pertinent data are shown in table 1. On this occasion, 1,910 c.c. of pericardial fluid

were withdrawn. The fluid appeared thinner than that obtained previously, although the color was unchanged; it contained 10,500 cells per cubic millimeter (7,800 red cells and 2,700 white cells). The differential count of the white cells showed 43 per cent polymorphonuclear cells, 51 per cent lymphocytes and 6 per cent monocytes. Examinations by direct smear, anaerobic and aerobic cultures, guinea pig inoculation

and cytologic study were again negative.

The patient was much less dyspneic immediately after pericardial aspiration. The next day (March 13) the heart sounds were more distinct, and a pericardial friction rub was audible. An intradermal test with old tuberculin 1:100 in dilution was negative after 48 hours. A PA chest x-ray showed a marked decrease in the size of the cardiac silhouette and an increase in the right hydrothorax. Two days later the patient developed rapid auricular fibrillation which reverted to sinus rhythm after the intravenous injection of 1 mg. of Digoxin. A PA chest x-ray on March 25 showed further accumulation of pericardial fluid. The third pericardial aspiration was performed on March 27, when 1,600 c.c. of pericardial fluid were removed and 400 c.c. of air injected. X-rays suggested a possible tumor nodule along the right border of the pericardium (figure 1C).

In view of the rapid recurrence of effusion and the suspicion of neoplasm, pericardiectomy was performed by Dr. E. B. Mahoney on April 4, 24 hours after removal of 875 c.c. of bloody pericardial fluid. When the sac was opened a moderate amount of fluid was present and the pericardium was markedly thickened, measuring 0.5 to 1 cm. The inner surface was covered with plastic exudate. The epicardium was also covered with a soft exudate which could be stripped away easily, revealing a gray, granular and oozing myocardial surface. Thorough exploration of the sac failed to disclose a tumor. The appearance was that of chronic inflammation. The exudate was stripped from both ventricles and the anterior surface of the auricles. The entire anterior pericardium was removed, as well as a large segment of the pericardium posterior to the phrenic nerve. Penicillin and streptomycin were given after operation, and the postoperative course was uneventful.

Pathologic examination showed acute and chronic pericarditis, with scar and granulation tissue, deposits of cholesterol and associated foreign body reaction. Examination of smears, anaerobic and aerobic cultures, and guinea pig inoculation of the specimens from visceral pericardium were negative. Cultures for fungi were also negative. PA chest x-ray on April 6 and 10 showed bilateral hydrothorax. The right border of the cardiac silhouette was normal and the left border indistinct.

On April 12 the patient's temperature became normal and he was discharged on April 15, the forty-sixth hospital day. The possibility of myxedema was ruled out by normal basal metabolic rate and protein bound iodine determination. He was followed in the Medical Out-Patient clinic and continued to improve. A PA

chest x-ray was taken on October 2 (figure 1D).

On October 13 the patient was quite comfortable. There was minimal distention of his jugular veins. The heart was slightly enlarged to the left and the heart sounds were distinct and regular. Breath sounds over the left lung field were still diminished, and a few moist rales were heard at both lung bases. Cardiac catheterization was performed on the same day, and the catheter was advanced into the pulmonary "capillary." Data pertinent to the determination of cardiac output and stroke volume, measurement of pressures and resistances, and analysis of the blood gases are presented in table 1.

On March 10, 1953, lung volume and its subdivisions were determined by the helium dilution method described by Meneely and Kaltreider.⁸ There was no evidence of pulmonary emphysema. When the patient was seen again on April 24, 1953, there was no distention of the neck veins and the examination of the lungs

was essentially negative.

DISCUSSION

The hemodynamic effects of pericardial effusion in animals and patients have been described by various investigators. 8-7, 9, 10 Evans et al. 9 have suggested the following sequence of events in the hemodynamics of acute pericardial effusion produced in animals: (a) increase in right ventricular diastolic, right atrial and peripheral venous pressures due to mechanical compression of the heart: (b) development of inflow stasis and decrease in cardiac output; and (c) fall in the mean arterial blood pressure. These changes are characteristic of acute cardiac tamponade. The same sequence of events probably occurs in patients with sudden development of pericardial effusion, such as following stab wound of the heart.

In patients with slow development of pericardial effusion there may be little or no evidence of cardiocirculatory embarrassment. Therefore, it has been suggested that the "alterations in the circulation are related to the pressure exerted

within the pericardium and not to the volume of fluid therein."

The patient reported here had had massive pericardial effusion for at least 15 months preceding his hospital admission. Apart from increasing dyspnea and edema during this period, his deterioration was remarkably slow. This chronicity of symptoms suggests a benign process and accords with the failure to demonstrate a definite etiologic factor, which included intensive search for evidence of tuberculous infection. Furthermore, the gradual onset of the effusion and the prolonged course might favor slow and progressive distention of the pericardial sac. To the knowledge of the authors the volume of pericardial fluid (up to 1,910 c.c.) aspirated from this patient is the largest reported during a single pericardial paracentesis of a living patient.

During the first pericardial aspiration, after removal of 150 c.c. of pericardial fluid, although the gradient between the mean right atrial and intrapericardial pressures was 12 mm. Hg, the pressure gradient at the point of the expiratory pause was only 1 mm. Hg. These gradients increased to 16 and 5 mm. Hg,

respectively, after 1,400 c.c. of pericardial fluid were withdrawn.

Before the second pericardial aspiration the low cardiac output (4.32 L./min.) was manifested by the wide A-V oxygen difference, indicating increased extraction of oxygen by the tissue. In addition, with a relatively rapid heart rate, the stroke volume was low. There was a distinct elevation in the right atrial, superior vena caval and peripheral venous pressures. Immediately after the removal of 1,400 c.c. of pericardial fluid a definite decrease in the mean right atrial and superior vena caval pressures was observed, although both the cardiac output and stroke volume failed to show a significant change. These findings suggest that in this case aspiration of a considerable amount of pericardial fluid caused prompt reduction of the venous and right atrial pressures, whereas improvement in cardiac index was insignificant and increase in stroke index was delayed (table 1).

The right atrial pressure obtained before pericardial aspiration did not show the characteristic W- or M-shaped pattern which has been observed in patients with chronic constrictive pericarditis. ^{11, 12} Hansen and associates ¹¹ have described a case of pericardial effusion with a right ventricular pattern different from that associated with constrictive pericarditis. Theoretically the right atrial and ventricular pressure patterns in constrictive pericarditis and massive pericardial effusion should be similar, because the fundamental disturbance in the circulation—obstruction of blood inflow to the right ventricle due to restriction of ventricular diastolic filling—is essentially the same. One difference may be that constrictive pericarditis interferes abruptly with diastolic filling, whereas

the pericardial fluid of an effusion may exert a cushion-like action.

Six months following pericardiectomy the patient's striking improvement was associated with little venous distention and almost normal mean right atrial pressure. However, the cardiac output at rest was unchanged. The stroke volume was definitely increased because of the slower heart rate. Thus, the patient was able to maintain the same cardiac output with a slightly elevated venous pressure and essentially normal heart rate, in contrast to the markedly increased venous and right atrial pressures and a relatively rapid heart rate before operation.

The elevated pulmonary artery and "capillary" pressures observed during the postoperative cardiac catheterization reflect some impairment of the blood flow through the left side of the heart. There was no clinical evidence of mitral valvular disease, frank left ventricular failure or chronic pulmonary disease to account for this. It is quite likely that some interference with diastolic filling of the left ventricle existed, perhaps due to residual pericardial and/or myocardial scarring. Elevated pulmonary artery and "capillary" pressures are constant findings in patients with constrictive pericarditis, sometimes even after pericardiectomy. 13, 14

SUMMARY AND CONCLUSIONS

- 1. Clinical and hemodynamic observations are reported on a patient with (a) massive pericardial effusion of 15 months' duration, and (b) central circulatory failure.
- 2. Three pericardial aspirations in three weeks yielded a total of more than 5,000 c.c. of pericardial fluid. On one occasion 1,910 c.c. were removed. Temporary symptomatic improvement occurred after each pericardial tap. Pericardiectomy revealed chronic inflammatory disease of unspecified cause, and was followed by remarkable clinical improvement.

3. The results of preoperative and postoperative cardiac catheterization are

presented.

 The pathogenesis of the associated hemodynamic abnormalities is discussed, and certain differences from changes seen in cases of chronic constrictive pericarditis are described.

ACKNOWLEDGMENT

The authors wish to express their appreciation and thanks to Mr. S. John Vernarelli and Miss Caroline Gouverneur for technical assistance, and to Mrs. Julia N. Gooding for preparing the manuscript.

BIBLIOGRAPHY

- Gauchet, H. W., and Katz, L. N.: Observations on pulsus paradoxus (with special reference to pericardial effusion); clinical and experimental, Arch. Int. Med. 33: 350, 371, 1924.
- Camp, P. D., and White, P. D.: Pericardial effusion: a clinical study, Am. J. M. Sc. 184: 784, 1932.
- Smith, H. L., and Willius, F. A.: Pericarditis. III. Pericarditis with effusion, Arch. Int. Med. 50: 192, 1932.

- Caughey, J. L., Jr.: A case of pericarditis with effusion; studies of venous pressure changes. Bull. New York Acad. Med. 13: 1, 1937.
- Stewart, H. J., Crane, N. F., and Deitrick, J. E.: Studies of the circulation in pericardial effusion, Am. Heart J. 16: 189, 1938.
- Fletcher, C. M.: Cardiac output in a case of pericardial effusion, Brit. Heart J. 7: 143, 1945.
- Warren, J. V., Brannon, E. S., Stead, E. A., and Merrill, A. J.: Pericardial tamponade from stab wound of the heart and pericardial effusion or empyema: a study utilizing the method of right heart catheterization, Am. Heart J. 31: 418, 1946.
- Mencely, G. R., and Kaltreider, N. L.: The volume of the lung determined by helium dilution. Description of the method and comparison with other procedures, J. Clin. Investigation 28: 129, 1949.
- Evans, J. M., Walter, C. W., and Hellems, H. K.: Alterations in the circulation during cardiac tamponade due to pericardial effusion, Am. Heart J. 39: 181, 1950.
- Adcock, J. D., Lyons, R. H., and Barnwell, J. B.: The circulatory effects produced in a patient with pneumopericardium by artificially varying the intrapericardial pressure, Am. Heart J. 19: 283, 1940.
- Hansen, A. T., Eskildsen, P., and Gotzsche, H.: Pressure curves from the right auricle and the right ventricle in chronic constrictive pericarditis. Circulation 3: 881, 1951.
- Yu, P. N. G., Lovejoy, F. W., Jr., Joos, H. A., Nye, R. E., Jr., and Mahoney, E. B.: Right auricular and ventricular pressure patterns in constrictive pericarditis, Circulation 7: 102, 1953.
- Scannell, J. G., Myers, G. S., and Friedlich, A. L.: Significance of pulmonary hypertension in constrictive pericarditis, Surgery 32: 184, 1952.
- Sawyer, C. G., Burwell, C. S., Dexter, L., Eppinger, E. C., Goodale, W. T., Harken, D. W., and Haynes, F. W.: Chronic constrictive pericarditis: further consideration of the pathologic physiology of the disease, Am. Heart J. 44: 207, 1952.

OBSTRUCTION OF THE SUPERIOR AND INFERIOR VENAE CAVAE IN THE SAME INDIVIDUAL*

By Robert Edgar Mitchell, Jr., M.D., and Jack L. Grindle, M.D., New Orleans, Louisiana

Thrombosis or obstruction of the superior vena cava is not infrequently encountered in clinical medicine. Likewise, thrombosis, obstruction, or ligation of the inferior vena cava is also encountered. However, the occurrence of obstruction of both the superior and inferior venae cavae in the same individual presents such problems of venous return that the following case is presented in some detail.

CASE REPORT

A 32 year old Negro male bartender was referred to Charity Hospital of New Orleans with the chief complaints of "shortness of breath and swelling of the legs and abdomen."

In August, 1948, swelling of the abdomen and left knee and minimal exertional dyspnea were noted. The patient was hospitalized by his local physician for 18

* Received for publication March 25, 1953.

From the Department of Medicine, Tulane University School of Medicine, and the Department of Surgery, Louisiana State University, New Orleans.

days and treated with dietary restriction of sodium, vitamins, protein supplements and diuretics. He was instructed to abstain from alcohol. (His average daily intake for the previous three years had been one pint of whiskey.)

In March, 1949, his alcoholic consumption was resumed (one-half pint whiskey per day), and no particular diet was followed. Abdominal distention, moderate exertional and nocturnal dyspnea, and enlargement of the left knee recurred. The patient was hospitalized for one month and received the same regimen as before. At discharge, there was only a trace of left pedal edema.

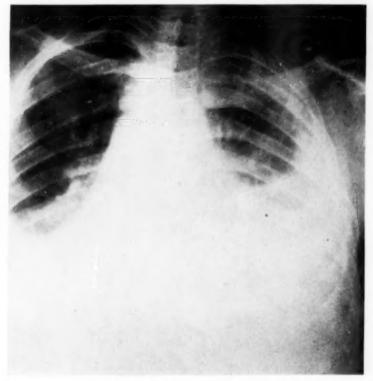


Fig. 1. Roentgenogram taken June 21, 1951 showing enlargement of the cardiac shadow, with a definite increase of the hilar and peripheral bronchovascular markings. There are a marked right pleural effusion and a less marked left pleural effusion.

In October, 1949, the patient developed severe ascites and bilateral edema of the legs, and marked exertional dyspnea. Mercurial diuretics were instituted again by his physician, with moderate response. This regimen was followed until October, 1950, when he was hospitalized with generalized anasarca. Weight had increased from the normal 176 pounds to 230 pounds. The same regimen was again instituted and he was discharged six months later weighing 185 pounds. He was immediately rehospitalized by another physician and digitalis was added to the regimen. When

the patient failed to respond to this treatment, he was referred on June 21, 1951, to Charity Hospital in New Orleans.

The patient weighed 250 pounds on admission and had a dull aching pain in the right side of the chest, exaggerated on inspiration. Thoracentesis yielded 30 c.c. of a dark red fluid and relieved the pain. With daily use of digitalis, diuretics and dietary sodium restriction his weight fell to 160 pounds. Cardiac catheterization was refused by the patient. He was then observed as an outpatient for one month.



Fig. 2. Roentgenogram of June 28, 1951, again showing marked right pleural effusion.

In October, 1951, he was re-admitted to Charity Hospital because of increasing edema and dyspnea.

Past medical history, family history, social history and review of his systems were all essentially noncontributory.

Physical Examination: Normal temperature, pulse and respiration. Blood pressures: Right arm, 118/60-0 mm. of Hg; left arm, 114/64-30 mm. of Hg; left leg, 136/90 mm. of Hg. Height, six feet two inches; weight, 185 pounds.

The patient appeared chronically ill. He walked with difficulty because of the extensive edema of the legs. The neck veins were distended in the erect position.

The chest revealed a marked inspiratory lag on the right side, with retraction in the fifth and sixth intercostal spaces on the left at the midclavicular line. There were decreased tactile fremitus, dullness to percussion, and absence of breath sounds from the right fifth interspace downward. Fine scattered moist râles were heard throughout the remainder of both lung fields.

Auscultation of the heart revealed an apical systolic murmur. The abdomen was markedly distended and a fluid wave was present. The liver could not be palpated but was percussed 5 cm, below the costal margin. There were large tortuous

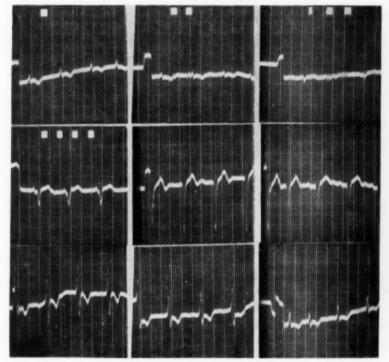


Fig. 3. Electrocardiogram, taken October 17, 1951, showing Leads I, II and III, and V1-V6.

veins in the abdominal wall around the umbilicus. These veins filled both from above and from below. Brawny, pitting edema was present in both legs and the scrotum.

Roentgenography: Chest x-rays revealed an enlarged cardiac shadow and an increase of hilar and peripheral bronchovascular markings. There was a right pleural effusion and a less marked left pleural effusion. Subsequent roentgenograms of the chest revealed no significant change (figures 1 and 2).

Fluoroscopy: Examination revealed a wide superior mediastinal shadow and minimal cardiac enlargement, with active pulsations of all borders. No calcium was

visible in the cardiac borders.

Electrocardiography: Several electrocardiograms revealed low voltage of QRS complexes in limb leads and in V., with definite evidence of heart disease (figure 3).

Laboratory Data: Packed cell volumes varied from 44 to 48. White blood cells varied from 5,750 to 17,500. Differential counts were normal. The urine was normal on repeated examinations. Pleural fluid was negative for tubercle bacilli on smear and culture. Cultures of blood, pleural fluid and urine were negative. Serum proteins varied from 4.8 to 7.5, and the icterus index from 8.5 to 13.0. A/G ratio was reversed. Cephalin flocculation and thymol turbidity tests were normal on several occasions. Circulation time (arm-to-tongue) was 16 seconds during his first Charity Hospital admission, and 30 seconds on the day of death. Mantoux tests were attempted but considered unsatisfactory because of the edema.

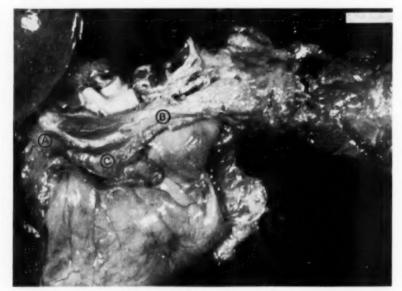


Fig. 4. The heart, showing very short inferior vena cava from liver (A), an organized thrombus in the superior vena cava (B), and thrombosed right auricle (C).

Venous pressures were as follows: Left arm, 430 mm. water; abdomen (large superficial vein near umbilicus), 400 mm. water; the pressure was also elevated in the dorsal pedal veins. Subsequent measurements revealed no change.

The same therapy was reinstituted. On the second hospital day the patient began spiking fever up to 105° F. daily, and continued to do so. Thoracenteses were attempted on three occasions but never yielded more than 60 c.c. of cloudy, straw-colored fluid. The edema persisted. On the ninth hospital day he became oliguric and there was a slight progressive weight gain. His condition gradually deteriorated and he died on his fourteenth hospital day.

Pathology Report: There was moderate edema of the face, arms, hands, thorax, back and abdomen, and massive brawny edema of the genitalia and lower extremities. Examination of the skin revealed a marked prominence of veins around the umbilicus. Another very prominent vein extended from the left femoral region to the umbilicus also.

Upon opening the chest it was found that the heart was enlarged only slightly (weight, 350 gm.). The pericardium was normal and contained approximately 30 c.c. of a clear yellow fluid. The superior vena cava was completely thrombosed from the level of the junction of the innominate vein down to and including the auricular appendage (figures 4 and 5). The thrombus was completely organized. On the posterolateral aspect of the superior vena cava, approximately two inches above the entrance into the heart, there was an area of caseous necrosis measuring two by one inches and filled with a white caseous material and some thick white semi-liquid material (figure 6). (A smear of this semi-liquid material demonstrated acid-fast organisms, and culture yielded Mycobacterium tuberculosis.) Further examination of the heart showed the epicardium to have a smooth, glistening surface. The left ventricle was much less dilated than the right. The myocardium was hypertrophied and firm. The coronary arteries were normal, as were their orifices.

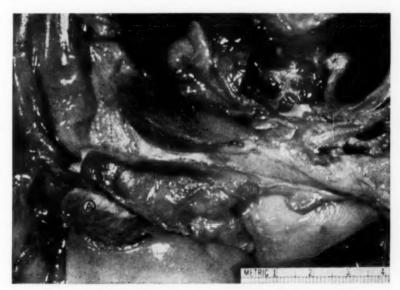


Fig. 5. Complete fibrosis and organization of the right atrium (A).

Examination of the left lung and thoracic cavity revealed approximately 50 c.c. fibrinopurulent fluid in the cavity. The lung weighed 450 gm. The pleural surface was smooth and no adhesions were present. The cut surface showed edema and congestion. The right thoracic cavity contained about 100 c.c. of fibrinopurulent material. The right lung was completely adherent to the chest wall by very dense adhesions, except anteriorly, and sharp dissection was necessary to remove the lung. Posterior to the right lung on the posterolateral portion of the thoracic cage was a large abscess cavity filled with serosanguineous material. The consistency of the lung was firm, the color gray-red.

The peritoneum had a smooth, glistening surface. One hundred fifty cubic centimeters of serous fluid were present in the peritoneal cavity, and there were

dense fibrous adhesions about the inferior vena cava.

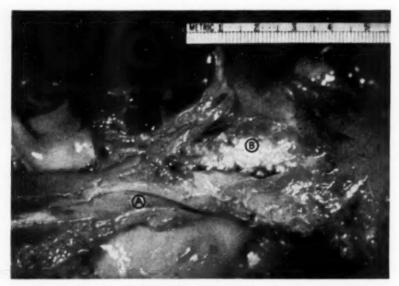


Fig. 6. Organized thrombus in the superior vena cava (A), and caseous necrosis at junction of the superior vena cava with the right atrium (B).



Fig. 7. Large umbilical vein (A) is seen entering the liver from the umbilicus. A probe is in the large dilated portal vein (B).

The liver weighed 2,000 gm. and was traversed by tremendously dilated veins, including a very large portal vein, which communicated within the substance of the liver with the superior superficial epigastric and the inferior superficial epigastric veins, which entered the abdomen at the umbilicus. The latter two veins converged at the umbilicus and formed a reopened umbilical vein, which in turn opened into a vein which communicated within the portal network and also emptied into the hepatic vein. This, in turn, emptied into the terminal 2.5 cm. of the vena

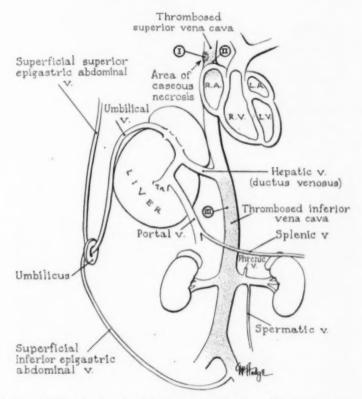


Fig. 8. Diagram showing the pathways of venous return. Microscopic sections have been made from portions marked I, II and III. These are shown in figures 9, 10 and 11 with accompanying descriptions (q.v.).

cava (inferior), which was all that remained patent in the inferior vena cava. The remainder of the inferior vena cava was an organized fibrous strand extending from the right auricle to the common iliac veins (figure 7).

One of the most puzzling problems was to establish the venous return from the kidneys. Blood from the left kidney drained from the renal vein into the spermatic vein and the network of veins about the surface of the kidney. Venous return from the right kidney could not empty into the spermatic vein, and apparently the venous

network about the right kidney was the only method of drainage. There were many dense fibrous adhesions about both perinephritic areas, and the anatomy could not be demonstrated satisfactorily. The right kidney weighed 350 gm., the left, 300 gm.



Fig. 9. Cross section through caseous area (as indicated in figure 8). The calcific, caseous and fibrotic nature of the lesion is well shown. Mycobacterium tuberculosis was demonstrated in this lesion.

The pancreas weighed 100 gm. and appeared normal. The spleen weighed 250 gm. and also appeared normal. The stomach and small and large intestines were grossly normal and revealed no nodules, ulcers or other lesions within any of the intestines. The mucosa of the rectum was congested and there were internal and external hemorrhoids. The bladder, prostate and testicles appeared grossly normal.

The arteries, including the aorta, were essentially normal. There were a few small scattered atherosclerotic plaques in the aorta.

DISCUSSION

There is apparently no agreement as to whether the circulation in the upper part of the body is slowed in cases of obstruction to the superior vena cava.¹⁸ Soloff ⁸ and Gray and Skinner ⁵ report prolonged circulation time, but others

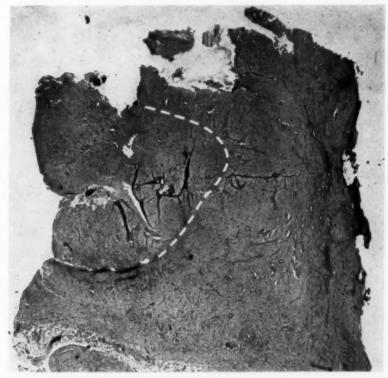


Fig. 10. Thrombosis of superior vena cava (retouched to show outline of vessel wall via broken white line), with scar tissue and granulation tissue about the wall. This section taken as indicated on figure 8.

(Lian and Abaza ¹⁹) report normal circulation time and high venous pressure to be diagnostic of the condition. According to Renbourn, ¹⁸ the collateral channels produced in obstruction of the superior vena cava depend upon whether this obstruction is superior or inferior to entrance of the azygos major. If superior, the main collaterals open into a patent portion of vena cava below the block, and collateral circulation time is relatively direct and not appreciably altered. Altschule et al.⁷ stated that in superior vena caval obstruction the circulation

time is delayed, and, further, that the slowing is on the venous side of circulation in the upper part of the body. Hitzig 14 concurs in these latter findings. In our case of thrombosis of both superior and inferior venae cavae in the same individual we noted a normal to moderate prolongation in circulation time. It is felt that measurements of circulation time are not of much value in this con-

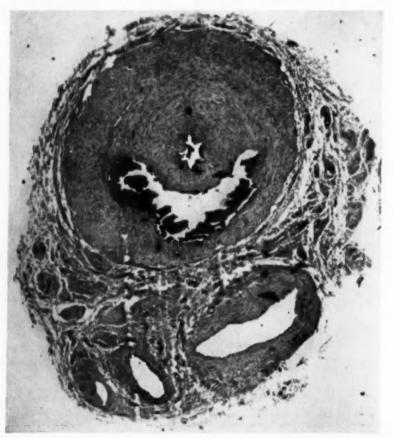


Fig. 11. Section through inferior vena cava (as indicated on figure 8), showing old fibrotic occlusion with calcific deposits and collateral channels about it.

dition, as any prolongation detected may be only an expression of the winding pathway of the blood. Hussey et al. 10 concur with this latter statement.

A series of 35 cases of superior vena caval syndrome reported by Hussey et al.¹⁰ lists the main causes as being aneurysm of the ascending aorta, bronchogenic carcinoma, metastasis to the mediastinum from carcinoma in other loca-

tions, and malignant lymphoma. They conclude that very little may be done in the way of treating the condition.

The resemblance of constrictive pericarditis to this condition is given in this report; however, it should be noted that there was no pulsus paradoxus and no low pulse pressure, and that the heart was not "small and quiet," although the latter condition is not necessarily present.

Cirrhosis of the liver was chiefly excluded clinically by the presence of cervical venous congestion, elevation of venous pressure in the upper extremities,

and laboratory studies of hepatic function.

Superior vena caval syndrome alone was excluded by the presence of generalized venous hypertension, cyanosis with prominent abdominal veins, and ascites. Inferior vena caval syndrome was also excluded by these latter findings.

BIBLIOGRAPHY

- Brown, A. L.: Complete occlusion of the superior vena cava by primary carcinoma of the lung, Arch. Surg. 21: 959, 1930.
- Barth, cited by Osler, W.: On obliteration of the superior vena cava, Bull. Johns Hopkins Hosp. 14: 169, 1903.
- Dana, H. W., and McIntosh, R.: Obstruction of the superior vena cava by primary carcinoma of the lung, Am. J. M. Sc. 163: 411, 1922.
- Ochsner, A., and Dixon, J. L.: Superior vena caval thrombosis, J. Thoracic Surg. 5: 641, 1936.
- Gray, H. K., and Skinner, I. C.: Constrictive occlusion of the superior vena cava, Surg., Gynec. and Obst. 72: 923, 1941.
- Pilcher, L. S., and Overholt, R. H.: Venous obstruction in the upper mediastinum, Ann. Surg. 100: 74, 1934.
- Altschule, M. D., Iglauer, A., and Zamcheck, N.: Respiration and circulation in patients with obstruction of the superior vena cava; cerebral factors in dyspnea and orthopnea, Arch. Int. Med. 75: 24, 1945.
- Soloff, L. A.: The syndrome of superior vena caval obstruction, Am. Heart J. 18: 318, 1939.
- Ehrlich, W., Ballon, H. C., and Graham, E. A.: Superior vena cava obstruction with consideration of the possible relief of symptoms by mediastinal decompression, J. Thoracic Surg. 3: 352, 1934.
- Hussey, H. H., Katz, S., and Yater, W. M.: The superior vena caval syndrome, report of 35 cases, Am. Heart J. 31: 1, 1946.
- Ferris, E. B., and Williams, R. W.: The clinical value of comparative measurements of the pressure in the femoral and cubital veins, Am. Heart J. 13: 431, 1937.
- Veal, J. R., and Hussey, H. H.: Use of "exercise tests" in connection with venous pressure measurements for detection of venous obstruction in upper and lower extremities, Am. Heart J. 20: 308, 1940.
- Armstrong, E. L., Coggin, C. B., and Hendrickson, H. S.: Spontaneous arteriovenous aneurysms of the thorax, Arch. Int. Med. 63: 298, 1939.
- Hitzig, W. M.: On mechanisms of inspiratory filling of the cervical veins and pulsus paradoxus in venous hypertension, J. Mt. Sinai Hosp. 8: 625, 1942.
- David, P., and Gratton, J.: Syndrome de la veine cava superieure, Union méd. du Canada 79: 257, 1950.
- Lutembacher, R.: Obliteration de la veine cave superieure et tumeur du mediastin, Presse méd. 47: 643, 1946.
- 17. Gravano, L.: Obliteracion cronica de la vena cava superior, Dia méd. 63: 2021, 1947.
- 18. Renbourn, E. T.: Thrombosis of the superior vena cava, Thorax 1: 257, 1946.

 Lian, C., and Abaza, A.: La dissociation de la pression veineuse et de la vitresse circulatoire, signe caracteristique de l'obstruction de la veine cave superieure, Bull. et mém. Soc. méd. d. hôp. de Paris 51: 750, 1935.

20. Jordan, H. E., and Kindred, J. E.: Textbook of embryology, 4th Ed., 1942, D. Appleton-

Century Company, New York.

 Lewis, W. L.: Gray's Anatomy of the human body, 24th Ed., 1944, Lea and Febiger Company, Philadelphia.

CARDIAC ANEURYSM WITH VENTRICULAR TACHYCARDIA: CASE REPORT AND BRIEF REVIEW OF THE LITERATURE *

By Edward Wasserman, M.D., Brideport, Connecticut, and Jacob Yules, M.D., Boston, Massachusetts

Because the clinical features are so indefinite, diagnosis of cardiac aneurysm is frequently overlooked. The following case illustrates an instance where the antemortem diagnosis was made by accumulation of certain physical signs, x-ray findings and electrocardiographic changes.

CASE REPORT

First Admission: A 67 year old retired plate glass worker was admitted to the

Boston City Hospital in June, 1949, because of weakness.

He had been well until two months prior to admission, when he noted the sudden onset of weakness, chills, fever and cough. He was treated for an upper respiratory infection, but weakness persisted. Chest pain, dyspnea and ankle edema were never noted. An electrocardiogram was suggestive of an "anterolateral myocardial infarction," and he was admitted.

The patient had not enjoyed good health during the previous 10 years, dating many complaints to 1939 when, while working, a glass plate was broken and he sustained a penetrating wound of his left anterior chest wall. Although this incident required no more than emergency treatment, he experienced subsequent frequent episodes of paroxysmal palpitations. These came on suddenly and disappeared "just as suddenly," after lasting for from three minutes to four hours. He was given maintenance digitalis for this condition. Two years prior to admission he had undergone a right lumbar sympathectomy, and, finally, a midthigh amputation of his right leg because of arterial insufficiency.

Additional history and review of systems were noncontributory.

Physical examination revealed the following significant findings: The patient was afebrile and in no distress. Crepitant rales were noted in his left lung field posteriorly. The point of maximal intensity was noted to be forceful and diffuse in the fifth left interspace at the left anterior axillary line, and an additional pulsation was noted 2 cm. medial to the apical impulse. His heart was enlarged at its apex to his left anterior axillary line by percussion in the fifth left interspace. The base was not widened. Auscultation revealed the heart sounds to be of good quality; the rhythm was regular, and the rate was 80/min. A soft apical systolic murmur was heard. Blood pressure in both arms was 120/60 mm. of Hg.

*Received for publication February 17, 1953.

From the Fifth and Sixth Medical Services (Boston University) of the Boston City Hospital.

There was a well healed amputation of his right lower extremity, with absent pulsations in his left leg. Peripheral vessels were noted to be tortuous and sclerotic.

Significant laboratory data revealed normal routine blood counts, urines and stools. Sedimentation rate varied inconsistently from 0 mm./hour to 30 mm./hour. Blood Hinton was negative, as were several blood cultures. Nonprotein nitrogen and fasting blood sugars were within normal limits.

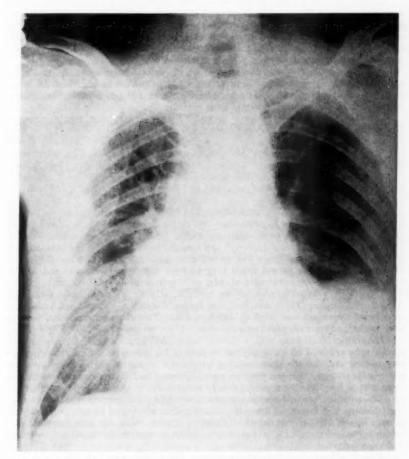


Fig. 1. Chest plate showing a bulge in the region of the apex of the left ventricle.

X-ray and fluoroscopy of his chest confirmed the clinical suspicion of a ventricular aneurysm at the apex of the left ventricle (figure 1).

Electrocardiograms revealed a normal sinus rhythm, rate 94; PR .15, and QS of .10. There were small R waves in Leads V₁-V₈, inclusive; deep Q waves were noted in Leads I, aVL, V₈, V₉ and V₈; ST segment elevations were present in Leads

V_{*}, V_{*} and V_{*}. Serial electrocardiograms over a five week period showed no change other than the presence of nodal premature beats on a single occasion.

The patient's hospital course was uneventful, with gradual improvement in his weakness. Therapy consisted of four weeks of bed-rest and anticoagulants. He was ambulated slowly, and was subsequently discharged on maintenance digitalis after five and one-half weeks.

Second Admission (four months later): The patient had been essentially well at home, except for a few episodes of palpitations, until the day before admission. At that time he noted the sudden onset of palpitations associated with stabbing left neck pain and dyspnea. This episode lasted only three hours. On the day of admission, shortly after arising, he had a sudden exacerbation of symptoms which persisted the entire day, causing him to seek admission.

Physical examination was the same as on his prior admission except that râles were noted at his right base. The liver edge was palpable one fingerbreadth below his right costal margin. The rate on admission was 160 per minute, immediately converted to 88 per minute by carotid sinus pressure.

Laboratory studies were again normal. X-ray of his chest was unchanged. Electrocardiogram revealed the development of an intraventricular block (QS = .12), but was otherwise unchanged.

The patient's hospital course was marked by two further episodes of palpitations, not associated with neck pain or dyspnea, which reverted immediately upon application of carotid sinus pressure. The administration of quinidine in small doses appeared to have prevented further attacks of tachycardia. The patient was discharged on quinidine after seven days.

Third Admission (nine months later): The patient did extremely well on medication until five weeks prior to admission. At this time he noted the sudden onset of sharp, vicelike substernal pain which radiated to his back, neck and left shoulder. This pain lasted 10 minutes before it spontaneously disappeared. He was seen by his family physician, who gave him an injection and kept him at bed-rest. During the ensuing period the patient noted progressively increasing weakness and breathlessness, but denied any recurrence of chest pain, orthopnea or ankle edema.

Physical examination revealed an afebrile, slightly cyanotic male with mild respiratory distress. There was moderate venous distention, and medium moist râles were heard over the lower third of both lung fields. Cardiac and abdominal findings were unchanged from the previous admission. Blood pressure was 110/85 mm. of Hg.

Laboratory data were within normal limits, and chest x-rays, fluoroscopy and kymography revealed no change in the contour of his aneurysm. Electrocardiograms at this time revealed the presence of a left bundle branch block, without any other appreciable change. Venous pressure on admission was 210 cm., and circulation time from arm to lung was 10 seconds; arm to tongue was greater than three minutes.

The patient's hospital course was characterized by satisfactory response to rapid digitalization and mercurial diuresis. Shortly after admission he was noted to have a heart rate of 150 per minute, which failed to respond to carotid sinus pressure until he was given sedation. He was discharged after seven days on maintenance digitalis and a low-salt diet.

Fourth Admission (two months later): The patient did well until two weeks before admission, when he noted increasing dyspnea, orthopnea and slight swelling of his ankles. He had taken his medication as directed, and denied chest pain or palpitations.

Physical examination revealed the recurrence of venous engorgement and increased pulmonary congestion. Cardiac findings were unchanged, but liver enlargement with associated tenderness was noted. He had minimal pitting ankle and sacral edema.

Laboratory data were normal. Chest x-ray and electrocardiograms were unchanged (figure 2-A).

His hospital course was uncomplicated, with rapid response to oxygen, bed-rest, mercurial diuresis and digitalis. He was discharged after two weeks on maintenance

digitalis, a low-salt diet and ammonium chloride.

Final Admission (11 days later): On the day of admission the patient noted the sudden onset of palpitations and a steady, moderately severe, nonradiating pain in his left axilla and in both elbows. This was accompanied by nausea, vomiting, sweating and dyspnea. Within four hours the pain and vomiting had disappeared, but his other symptoms persisted until the time of admission.

Physical examination revealed an anxious, cyanotic white male in moderate respiratory distress. There was marked venous distention, and an irregular cervical pulsation was noted in both supraclavicular regions. Lung fields were clear. His heart was enlarged to the left anterior axillary line and the apical impulse was described as heaving and diffuse. Auscultation revealed a regular rhythm with a rate

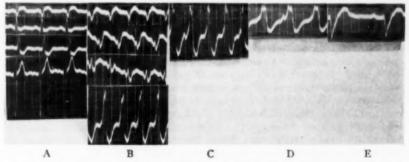


Fig. 2. A. Leads I, II, III and third right taken prior to last admission and showing normal sinus rhythm. B. Leads I, II, III and third right taken on last admission before treatment and showing ventricular tachycardia. C. Third right lead showing ventricular tachycardia after treatment with Pronestyl. D. Third right lead showing idioventricular rhythm immediately following course of quinidine. E. Third right lead showing normal sinus rhythm with 2:1 block three hours after omitting quinidine.

of 140. Heart sounds, although slapping in character, varied from loud to moderate in intensity. There was a soft blowing apical systolic murmur, and blood pressure was 90/70 mm. of Hg. The liver was enlarged but nontender.

Laboratory data revealed normal blood counts and urinalysis. Electrocardiogram

on admission revealed a ventricular tachycardia (figure 2-B).

Following hospital admission the patient's anxiety and cyanosis lessened. He was given oxygen and 1,000 mg. of Pronestyl intravenously, without any effect on his abnormal rhythm. He was then given a trial of oral Pronestyl for a total dose of 6.25 gm. over a two day period, but this failed to convert his ventricular tachycardia (figure 2-C). All medications were then discontinued and he was given 1 gm. of quinidine over a 12 hour period; this also failed to have any effect. On the following day a total of 1.8 gm. of quinidine was administered in divided doses, again without appreciable effect other than to cause nausea and a slight increase in QRS complex from .17 to .18. On his final hospital day he was given a total of 3 gm. of quinidine in ascending doses over an eight hour period. An electrocardiogram following the final dose of quinidine revealed an idioventricular rhythm with a ventricular rate of

88 per minute (figure 2-D). Three hours later a tracing showed a normal sinus rhythm with 2:1 A-V block and a ventricular rate of only 43 (figure 2-E). Shortly thereafter the patient suddenly went into peripheral circulatory collapse and died.

At necropsy the heart weighed 900 gm. The left ventricle presented a large bulge 5 cm. by 8 cm. over the anteroapical surface, which was firm and covered with fibrous adhesions to the parietal pericardium. The myocardium in the septum showed numerous small white scars near the base and several large white dense scars near the apex. The myocardium near the area of the bulge on the left ventricle was extremely thin but revealed no red or white discoloration. The left ventricle was markedly dilated over the thin bulging portion and was filled with a firm, gray, laminated thrombus which completely filled the bulging portion. Near the edge of the thrombus, where it adjoined normal endocardial surface, was a thin, red, recent clot. There was moderate endocardial thickening over the left ventricular surface of the septum. The valves were not remarkable. The right coronary artery revealed moderate atherosclerotic deposition without marked narrowing. The left coronary artery was completely occluded in its anterior descending portion, and the circumflex branch was very narrowed. Theere was no evidence of recent myocardial infarction.

DISCUSSION

The formation of a cardiac aneurysm is one of the less frequent complications following myocardial infarctions. The literature reveals an incidence varying from 9 per cent 1 to as high as 37 per cent.2 The correct diagnosis is occasionally made, but usually it is first discovered by x-ray or postmortem examination. Crawford has defined a cardiac aneurysm as a "permanent localized bulging, or a well marked localized expansion during systole beyond the contour of the rest of the heart." In the majority of cases cardiac aneurysm follows myocardial infarction. The intraventricular pressure may cause the formation of an aneurysm as healing with fibrosis progresses, unless the scar becomes strong enough or is reinforced by mural thrombi and adherent pericardium.4 Resultant fibrosis and thinning occur, which leads to a localized cardiac dilatation.⁵ Occlusion of the descending branch of the left coronary artery, with consequent aneurysm of the anterior surface of the left ventricle or apex, is the usual pathologic finding. The apex, being most distant from the adequate blood supply, is involved most. In a large series of cases, Applebaum and Nicholson found almost all the aneurysms located in the left ventricle.6 Forty-eight of 49 cases in another series revealed involvement of the lateral or anterior portion of the apex of the left ventricle.7 The upper portion of the intraventricular septum is infrequently the site of aneurysm formation.8 Other rarer causes of cardiac aneurysm are trauma, bacterial infection of the myocardium from either abscess or embolus, syphilitic gumma and rheumatic myocarditis. Calcification in the wall of such aneurysms has been reported.4.9

There is general agreement in the literature that about two thirds of all cardiac aneurysms occur in the male sex.^{10, 11} This is probably due to the higher incidence of coronary occlusions among males.

The average period elapsing between the attack of myocardial infarction and the development of aneurysm has been reported as varying from one week 12 to more than 17 months.1

Because the clinical features are so indefinite, the diagnosis of cardiac aneurysm is difficult. There is in most cases a history of a previous episode of

myocardial infarction and, frequently, of an inadequate period of bed-rest. 18, 14
Experiments have shown that dogs who were exercised following coronary artery ligation developed aneurysms, while control dogs, given an adequate rest

period, had well healed scars and developed no aneurysms. 16

Symptoms, when present, are those of cardiac decompensation. Pain or localized tenderness over the precordial area has been noted by only a few authors.^{8, 9} These patients often undergo repeated episodes of congestive failure, and compensation is usually difficult to achieve.⁹ It is thought that aneurysm itself does not alter the prognosis. The deciding factor appears to be the functional capacity of the remainder of the ventricle.⁵ Some patients have survived as long as 17 years following the development of a ventricular aneurysm.⁵

Libman and Sacks described as a diagnostic sign an abnormal palpable pulsation separate and distinct from the apical pulsation, and located between the sternum and apex.¹⁸ Gallop rhythm in association with a dull first heart sound, together with a pulsation distinct from that of the apex, has been considered diagnostic of cardiac aneurysm.¹⁷ Parkinson and co-workers ¹ described in most of their cases an outwardly displaced apical impulse which was diffuse, forcible or heaving. Many different physical signs have been described but most of them have received little support in the literature. Most authors agree that there are no characteristic murmurs due to cardiac aneurysm.¹³ The blood pressure is variable. In 45 cases collected from the literature the average was found to be 130/70.¹

Various electrocardiographic patterns have been described, but it would appear that none is diagnostic of cardiac aneurysm and that the tracings merely suggest preceding myocardial infarction.²⁹ These changes have been reported to persist from months to years.^{18, 18} Right axis deviation has been found frequently in some series of cases.^{18, 19} A recent report by Steven ²⁰ has stressed that QS complexes, together with persistent S-T elevation in one or more precordial leads, strongly suggest underlying ventricular aneurysm. Others have

also noted this finding.81,82

The diagnosis of cardiac aneurysm depends mostly on x-ray findings. The most characteristic feature is a localized bulge on some portion of the contour of the left ventricle. The heart is most often enlarged to the left and the apex appears blunted, giving the heart a rectangular or square appearance, because the aneurysm frequently involves the lower half of the left ventricular contour.¹ The aneurysmal pulsations, visualized by fluoroscopy or kymography, may be strong or weak, systolic or contrapulsile, synchronous or asynchronous. However, asynchronicity with contrapulsile pulsation is seen in most cases.¹8

Cardiac aneurysms rarely rupture. Congestive failure or myocardial infarction is the usual cause of death. Occasionally cerebral embolism occurs

from a dislodged fragment of clot within the aneurysm.4

There are several points worthy of emphasis in the present case report. The patient had sustained a penetrating wound of his chest 10 years prior to his initial myocardial infarction. It is known that trauma of the thorax as well as coronary occlusion may be the cause of a cardiac aneurysm. Both of these etiologic factors were elicited in this patient's history. Subsequent to the episode of chest trauma he noted occasional brief episodes of palpitation, for which he was given a daily dose of digitalis. Digitalis may cause ventricular tachy-

cardia,28 and we can only speculate as to what rôle, if any, it played. These episodes of palpitation may actually have been periods of ventricular tachycardia.

During the patient's first hospital admission the presence of a pulsation just medial to the apical thrust was noted, similar to that described by Libman. X-ray of the chest at this time confirmed the presence of a large cardiac aneurysm (figure 1). On the second admission he probably had an episode of paroxysmal auricular tachycardia, since it responded rapidly to carotid sinus pressure. The electrocardiograms during these admissions revealed persistent elevation of the S-T segments in Leads V_{4.5} and 6. This has recently been emphasized as diagnostic of cardiac aneurysm. The second, third and fourth hospital admissions were necessitated by progressively severe and increasingly resistant episodes of congestive failure. It is known that patients with cardiac aneurysm frequently develop heart failure, and that compensation is difficult to achieve.

During his final admission the patient developed paroxysmal ventricular tachycardia (figure 2-B). A changing intensity of the heart sounds was noted at this time. Levine 22 has described this sign in the clinical diagnosis of this arrhythmia. Our patient was first given intravenous Pronestyl, then oral Pronestyl, without affecting the ventricular tachycardia (figure 2-C). Pronestyl, the amide of procaine, has been studied extensively by Mark et al.24 Its action is probably due to a direct depressant action on ventricular muscle. On the third, sixth and seventh hospital days the patient was given frequent amounts and, finally, ascending doses of oral quinidine. He was given a total of 85.5 gr. of this drug, and, following the last single dose of 15 gr., his rhythm was converted to an idioventricular type (figure 2-D). At this point quinidine was omitted, and three hours later, just prior to death, an electrocardiogram revealed normal sinus rhythm with a 2:1 A-V block (figure 2-E). The duration of the QRS complexes increased from 0.18 second at the onset of the ventricular tachycardia to 0.21 second on the final tracing. Quinidine is a valuable drug in the treatment of ventricular tachycardia.^{26, 80} However, because of the danger of ventricular fibrillation and cardiac standstill with overdosage.26 it has been stressed that quinidine therapy should be omitted when the QRS interval becomes too prolonged.27 Since the intravenous administration of quinidine is a hazardous procedure,23 intramuscular quinidine is now advocated as a safe parenteral method of choice.26 It is possible that the amount of quinidine employed was responsible for the patient's death by causing gradual irreversible prolongation of the QRS interval.

SUMMARY

 A case is presented of cardiac aneurysm, substantiated by necropsy, with development of ventricular tachycardia. The most likely etiologic factor was myocardial infarction, although aneurysm secondary to chest trauma could not be excluded.

The diagnosis in this case was suspected clinically by the presence of certain physical signs and x-ray findings.

3. A partial review of the literature is included in summarizing the pathogenesis, pathology, clinical features, roentgenologic manifestations, and electrocardiographic changes of cardiac aneurysm.

BIBLIOGRAPHY

- Parkinson, J., Bedford, E. E., and Thomson, W. A. R.: Cardiac aneurysm, Quart. J. Med. 31: 455-478, 1938.
- Scherf, D., and Boyd, L. J.: Cardiac aneurysm, M. Clin. North America 25: 919-927, 1942.
- 3. Crawford, J. H.: Aneurysms of the heart, Arch. Int. Med. 71: 502-515, 1943.
- Bogoch, A., and Christopherson, E. F.: Calcified cardiac aneurysms, Ann. Int. Med. 32: 295–308, 1950.
- 5. Berman, B., and McGuire, J.: Cardiac aneurysm, Am. J. Med. 8: 480-489, 1950.
- Applebaum, E., and Nicholson, G.: Occlusive disease of the coronary arteries, Am Heart J. 10: 662, 1935.
- Schwedel, J. B., and Gross, H.: Ventricular aneurysm, Am. J. Roentgenol. 61: 32-36, 1939.
- 8. White, P. D.: Heart disease, 3rd Ed., 1947, The Macmillan Co., New York, pp. 595-598.
- 9. Berk, L. H.: Cardiac aneurysm, Am. Heart J. 17: 569-580, 1939.
- Levine, S. A., and Brown, C. L.: Coronary thrombosis: its various clinical features, Medicine 8: 245, 1929.
- Mallory, G. K., White, P. D., and Salcedo-Salger, J.: The speed of healing of myocardial infarction: a study of the pathological anatomy in 72 cases, Am. Heart J. 18: 647-671, 1939.
- Shookhoff, C., and Douglas, A. H.: A case of coronary occlusion with roentgenographic evidence of early development of an aneurysm of the left ventricle, Am. Heart J. 7: 95 1931
- 13. Dressler, W., and Pfeiffer, R.: Cardiac aneurysm, Ann. Int. Med. 14: 100-121, 1940.
- 14. Ball, D.: Aneurysm of heart, Am. Heart J. 16: 203-218, 1938.
- Sutton, D. C., and Davis, M. D.: Effects of exercise on experimental cardiac infarction, Arch. Int. Med. 48: 1118-1125, 1931.
- Libman, E., and Sacks, B.: Case illustrating leukocytosis of progressive myocardial necrosis following coronary artery thrombosis, Am. Heart J. 2: 321-326, 1927.
- Libman, E.: Affections of the coronary arteries, Interstate Post-Graduate Medical Association of North America Proceedings, Indianapolis, Indiana, p. 405, 1932.
- Gross, H., and Schwedel, J. B.: Clinical course in ventricular aneurysm, New York State J. Med. 41: 488-491, 1941.
- Eliaser, M., and Konigsberg, J.: Electrocardiographic findings in cases of ventricular aneurysm, Arch. Int. Med. 64: 493-504, 1939.
- Steven, R. A.: Electrocardiographic findings in cardiac aneurysm, Ann. Int. Med. 34: 747-758, 1951.
- 21. Fisher, R. L.: Cardiac aneurysm with rupture, Am. Heart J. 30: 133-140, 1945.
- Levine, S. A.: The clinical recognition of paroxysmal ventricular tachycardia, Am. Heart J. 3: 177, 1927.
- Armbrust, C. A., Jr., and Levine, S. A.: Paroxysmal ventricular tachycardia: a study of one hundred and seven cases, Am. J. Med. 1: 28, 1950.
- Mark, L. C., Berlin, I., Kayden, H. J., Rovenstein, E. A., Steele, J. M., and Brodie, B. B.: The action of procaine amide on ventricular arrhythmias, J. Pharmacol. and Exper. Therap. 98: 21, 1950.
- Pordy, L., Kolker, J., and Levy, H.: Paroxysmal ventricular tachycardia of prolonged duration, Am. J. Med. 10: 254, 1951.
- Schwartz, S. P., and Jezer, A.: The action of quinine and quinidine on patients with transient ventricular fibrillation, Am. Heart J. 9: 792, 1934.
- Reich, N. E.: Successful use of a massive dose of quinidine in a case of intractable ventricular tachycardia, Am. Heart J. 28: 256, 1944.

- Blinder, H., Burstein, J., Horowitz, W., Gerish, E., and Smelin, R.: Studies on the effects of parenteral quinidine administration, Arch. Int. Med. 86: 917, 1950.
- Moyer, J. B., and Hiller, G. I.: Cardiac aneurysm: clinical and electrocardiographic analysis, Am. Heart J. 41: 340, 1951.
- 30. Gold, H.: Quinidine in disorders of the heart, 1950, Paul B. Hoeber, Inc., New York.
- Ford, R. V., and Levine, H.: The electrocardiographic clue to ventricular aneurysm, Ann. Int. Med. 34: 998, 1951.
- Evans, E.: Ventricular aneurysm a cause of persistent RS-T segment displacement, Ann. Int. Med. 34: 1048, 1951.

EDITORIAL

THE RÔLE OF THE INTERNIST

To understand the rôle of the physician in any age is to understand the culture of that period. For he more than any other in all stages of our painful progress from savagery to civilization epitomized his times. When a culture developed and bloomed, the physicians rose with it, in fact often led and vitalized the movement, and the decay of great civilizations is more accurately measured by the degradation of the healing art than by any other yardstick. His rôle reflected in a most profound way the beliefs, the knowledge and the morals of the times and changed as these mores changed. In tune with his times he has been priest, simple craftsman, philosopher, biol-

ogist and now must be perforce social scientist.

When all disease was mysterious, all manifestations of nature incomprehensible and often malign, man looked to supernatural cures for his ills and the rôle of physician was that of priest—the familiar tribal shaman, the medicine man of the American Indian, the Levite of the ancient Hebrew, the high priest of Apollo the healer. The subtle Greek invented specialization even in those theistic days and Apollo's monopoly in time was divided among many gods; Hygeia was the goddess of health (the patron of preventive medicine if you will). Artemis was devoted to gynecology and pediatrics, Panacea was the healer of ills, Aphrodite was concerned with sexual things. Poseidon, Hera, Pan, Dionysus, Persephone, and Cerberus were all moved into the picture with a resulting fragmentation curiously prophetic of the infinite specialization of today. Asclepius a real tangible man became the symbol of the god, became himself deified and by the time of Alexander there were three hundred Asclepian temples in Greece.

When the great empirical system of Hippocrates replaced the cult of Asclepius, the physicians turned from incantations, prayers and sacrifices to diet, drugs, and hygienic practices and became as described in the words of Homer, "craftsmen of the people." The natural history of disease was portrayed with great insight in "The Prognostics," the supernatural was discounted. Occupational therapy was prescribed for the idle rich, fees

were charged rather than offerings received.

And this period passed. Under the influence of Plato, Aristotle and Theophrastus philosophy became the preoccupation of the intelligentsia and the physician once priest, then craftsman, became philosopher. The identity of man with the universe was stressed, analogies were drawn from the anatomy and physiology of animals and applied to man. The Hellenistic physicians studied Plato and Aristotle, set up dogmata, and reasoning from them by the inductive method applied the results to human ills.

Galen's eclecticism permitted him the philosophical approach but did not disdain the craftsmanship; but more importantly he reflected the teleological 958

viewpoints of the middle ages, the Creator dominated the scene in the life of the times, divine determinism dominated medical thinking and the physician became as before the exemplar and prototype of the man of his age.*

The analogy can be carried through the age of biological materialism, of scientific skepticism to our own disturbing age of atomic disintegration and social turmoil. For our time the internist, not alone, but principally, is the physician. He more than any other specialist will be regarded as the prototype of these times, will be studied by the historian and the student of ideas for an understanding of our culture. It is well that we should

regard ourselves in this light.

There was a time when the preëminence of the internist, naturally clearly understood by this audience, was recognized and accepted by all. There is preserved the picture of our lordly predecessor, the physician of medieval times, calling upon his titled but obsequious patient, followed by his train of humble satellites, the barber, the surgeon, the urine taster. It was not for his delicate hands to touch the cadaver—the dissection was done at his direction by the gelder of hogs. He wore the schoolman's academic robes. He spoke the Latin of the universities, and quoted in Greek from Aristotle or Hippocrates and no man ventured disagreement or dissent. We are come into a less enlightened age. And now we must reëxamine and perhaps justify our rôle. It is now not only a definition of the boundaries between medicine and surgery which was so learnedly discussed in 1904 in the magnificent monograph of Sir Clifford Allbutt (who concluded, by the way, that the use of the hypodermic needle was not beneath the dignity of the physician even though it involved pricking the skin) but defining as well the relationship of the internist to the apparently limitless number of subspecialties into which medicine has become fragmented. There is indeed reason for inquiry into the proper rôle of the internist in this intricate situa-There is need indeed for a clear appreciation, on the part of the internist, of the responsibility which is quite properly his for restoring and maintaining order in the face of threatened confusion.

I suppose I am an internist because I believe the internist is the most important man in the medical team. But I know I must yield in glamor (and income) to the surgeon; in the savings of lives to the public health man, to the radiologist in diagnostic precision, to the psychiatrist as an inspiration for modern literature. There are technicians whose manual dexterity is my envy and despair, medical physicists who speak a tongue obviously erudite, but completely incomprehensible to me. All this makes for humility. Yet I come to the conclusion that the internist is the most important man on the medical team. It is not despite, it is because of these many wonderful advances by such diversely gifted men that the rôle of the internist has become more important.

^{*}The foregoing in part is a paraphrase of a monograph by Ilza Veith called "The Physician-Priest, Craftsman, or Philosopher?", published by the Indian Institute of Culture.

EDITORIAL 959

The very complexity of modern medical science requires the internist more and more frequently to assume these three important functions, first that of coördination, second that of integration, and third that of interpretation. It is not an easy rôle but it is a vital one. To be sure the picture of the internist at the head of a train of subservient satellites must be discarded and replaced. We see him now rather as the hub of a wheel whose spokes radiate in all directions, controlling these spokes in a sense but moved by them, revolving with them, and moving forward with the whole.

Just as there are the three important functions, integration, coördination and interpretation, so also there are three areas in which these functions are exhibited, that of the patient, of the profession, and of society. Integration means the achievement of the integer—of unity. The centrifugal forces operating in medicine today resemble those described by the modern astronomer as he plots our expanding universe. These forces threaten such dispersion of the various disciplines which make up medicine today as to lead to complete disintegration. The internist must supply the centripetal, cohesive force of gravity to pull these divergencies together again into one stable solar system. This is the rôle of integration.

Wiener in his remarkable book on Cybernetics touched upon the waste which is inevitable when scientists in one field are denied the benefits of the discoveries and ideas of those in another. The application to medicine today is precise and striking. The process of bringing these people together, of using the discoveries in one field for the benefit of all is what is meant by

coördination and it is the second great function of the internist.

All this needs communication, exposition, explanation, not only from doctor to patient, but from doctor to doctor within the profession, and from profession to society, and let me add not infrequently from society to the profession. This is the third function, interpretation, which I would assign to the internist.

These functions in varying degress, and of course with many others as well, are exhibited in the three areas to which we have referred.

For the patient the exercise of these functions means that the internist becomes the guide for his patient through the medical maze in which he might well be lost. He integrates the factors of heredity and environment, of nutrition and emotional stress, and of all past and present systemic disorders, together with the personality of his patient. He becomes in short the personal physician. And this ancient rôle, so precious in our past, is even more needed in these days. The internist almost alone among the many specialists has—or he should have—the aptitudes necessary to become the personal physician. Of course among these aptitudes perhaps the most important is diagnostic acumen in the widest sense. This encompasses not only the ability to name the specific disease from which the patient suffers but the ability as well to understand and evaluate all the factors in the patient's situation which will affect his reaction to the disease. This involves in a

960

personal, but for the patient a vital way, the exercise of the three functions we have described. The internist brings together all the factors which bear on the problem at hand, which is integration, he coördinates the findings of his colleagues with his own observations, and he interprets these things to the patient both by what he says and by his therapy. At this point I should like to stress—it hardly seems necessary—the tremendous importance of the control and direction of psychic forces, not only for treatment but particularly for the prevention of neurotic disturbances, in order to make the point that this is one of the rôles that should be assumed by the internist, not the psychiatrist. But all these points can be summed up by saying that the internist should be the personal physician and with rare exceptions the

personal physician should be an internist.

The desirability of integration and coordination within the profession is too obvious to require comment, and in this group I think that it would he agreed that the internist is the one to do the job. We must assume more responsibility for the integration of our already dangerously fragmented profession. The rôle of the internist is like that of the conductor of a symphony orchestra. It is for him to see that harmony and not discord results from the coördinated activities of the individual performers-including the prima donnas, if such there be in the case. There is an added and often neglected obligation to our fellows to see that due credit and recognition are given to those who deserve it. Many an internist smugly takes the credit for a brilliant diagnosis which was in fact made not by him but by some completely anonymous roentgenologist or clinical pathologist. We must of course be ready to help our fellow practitioners at every opportunity but we must also be ready to accept help when we need it and to give credit to our helpers. It is well too for us to have the wit to know when we need help. The internist must not arrogate to himself arbitrary or autocratic controls but he must in all humility accept his rôle as integrator and coordinator within the profession.

And finally it is the internist more than any other who should recognize the tremendous and growing impact of medicine upon society. The sociologists, the economists, the biologists are becoming increasingly aware of this. Too often, immersed as we quite properly should be in the problems of individual patient care, we ignore the implications of our activities upon the welfare of mankind. William Osler and others of his intellectual caliber did not fall into this error. By training, by experience and most of all by a philosophy and mental discipline which is characteristic, the internist is better equipped to understand these problems than any other specialist. The obligation to interpret our art to the people rests largely upon the internist and we should accept it. The ability to coördinate our activities with those of others interested in the welfare of mankind is most likely to be found in the ranks of the internist. It is necessary for us to

EDITORIAL 961

consider what we are doing to society along with what we are doing for

These then are the roles of the internist, for the patient, a councilor and guide; for the profession, an integrator and coördinator; for society, a liaison agent, interpreter and leader.

It calls for all our wit.

It calls for more than wit. It calls for character. It is not enough that we regard ourselves as indicators of the great social chemical reactions which are taking place in society. We are more than indicators—we are rather powerful enzymes, catalysts of tremendous potency which may well determine the direction mankind takes. It is by no means inevitable that it will be forward. The possibility of wholesale destruction of the physical life of the planet is clearly present in the potential of atomic fission. The possibility of complete degradation of the human races through the operation of unfavorable genes, injudiciously preserved, is equally present. Loss of human liberty, destruction of human dignity have already become a reality for half of the human race. The physician—primarily the internist—must add these concerns to the many others with which he is burdened.

RUSSEL V. LEE. M.D.

REVIEWS

Normal Blood Pressure and Hypertension: New Definitions. By ARTHUR M. MASTER, M.D., Cardiologist, The Mount Sinai Hospital, New York, etc.; Charles I. Garfield, M.D., Research Assistant in Cardiology, The Mount Sinai Hospital, New York; and Max B. Walters, M.D., F.R.C.P. (Can.), Member, Heart Station, Vancouver General Hospital, Canada, etc. 144 pages; 24 × 15 cm. Lea & Febiger, Philadelphia. 1952. Price, \$4.00.

The authors have painstakingly presented the arguments for a revision of our concepts of normal blood pressure. Although their selection of material for statistical analysis may be subject to some criticism, they have rather convincingly demonstrated that age and sex significantly influence the level of blood pressure. Probably the most significant contribution of this work is that they have presented a range of normal blood pressures for the ages 16 to 65 in both sexes, rather than a mean.

A careful perusal of this text should do a great deal to alleviate the unwarranted therapy for a condition manifested solely by blood pressure readings above an arbitrarily fixed normal. It is recommended reading for physicians and students.

S. T. R. R., JR.

Clinical Diagnosis by Laboratory Methods. 12th Ed. By James Campbell. Todd, Ph.B., M.D., Late Professor of Clinical Pathology, University of Colorado School of Medicine; Arthur Hawley Sanford, A.M., M.D., Emeritus Professor of Clinical Pathology, The Mayo Foundation, University of Minnesota, etc.; and Benjamin B. Wells, M.D., Ph.D., Professor of Medicine, Department of Medicine, University of Arkansas. 998 pages; 24 × 16 cm. W. B. Saunders Company, Philadelphia. 1953. Price, \$8.50.

This volume is the twelfth edition of the well known laboratory text by Todd and Sanford. This edition is published with the collaboration of Dr. Benjamin B. Wells as coauthor.

The form and contents of the book are little changed, including sections on urine, blood, clinical chemistry, feces, parasitology, bacteriology, serology, mycology, skin tests, and body fluids.

It remains an adequate text for general use, but many concepts of disease and their relationship to laboratory tests are not fully explained. Recent advances in theory and laboratory confirmation of certain processes notably blood coagulation, have been omitted.

This book should be of value to those requiring information about performance and interpretation of routine laboratory tests. This information will require supplementation in specialized fields.

A. M. B.

Synovial Fluid Changes in Joint Disease. By Marian W. Ropes, M.D., Associate Physician, Massachusetts General Hospital, etc.; and Walter Bauer, M.D., Chief of Medical Services, Massachusetts General Hospital, etc. 150 pages; 24.5 × 16 cm. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Massachusetts. 1953. Price, \$4.00.

This monograph is the result of 20 years of study and evaluation. The authors, believing that joint fluid of normal cattle was analogous to normal human joint fluid, and easier to obtain, made a number of studies to develop a series of "normal" levels for synovial fluid.

REVIEWS 963

The study then proceeds to the abnormal, dealing with variations in characteristics of synovial fluid in pathological states, and includes complete bacteriological, cyto-

logical, enzymatic and chemical changes.

On the basis of these studies the discussion of abnormal fluid continues and is divided into the traumatic group and the rheumatoid arthritis and infectious disease groups. Similarities and differences are then pointed out in detail. A mass of statistical data, with charts and tables, is offered and discussed. A very complete bibliography is also included.

This book, if the "norm" studies on cattle are accepted as comparable to the human, is a classic and very complete. It is too technical for the average practitioner

but invaluable to students of arthritis and orthopedic conditions.

L. A. K.

Clinical Cardiology. By 33 authors; edited by Franklin C. Massey, M.D., Assistant Professor of Medicine, Hahnemann Medical College, Philadelphia, Pa. 1100 pages; 15.5 × 23.5 cm. The Williams and Wilkins Co., Baltimore. 1953. Price, \$13.50.

There are already several excellent textbooks of cardiology on the market. This latest addition to the list is not without its merits and its defects. The particular purpose of this contribution is to give allied specialties adequate representation in such a textbook; to this end there are detailed sections on pediatrics, metabolism, surgery, anesthesiology, obstetrics and psychiatry as related to cardiology. Otherwise the text govers the same field with similar thoroughness as other reputable volumes on the subject.

There is included a helpful summary of congenital cardiac lesions and of the modern maneuvers employed in their diagnosis, followed by 100 pages devoted to cardiac surgery. Taking these chapters as a unit they probably represent a uniquely

complete and up-to-date coverage of these progressive subjects.

The authors, 15 of whom are on the faculty of the Hahnemann Medical College in Philadelphia, for the most part do their job well. But there are so many minor deficiencies that one gets the impression that on the whole the work is sub-standard. There are a phenomenal number of misprints—which suggests indifference in editing. A host of trivial criticisms could be made: for example, in the section on the arrhythmias the electrocardiographic changes of bundle branch block are outlined without mention of the characteristic findings in the precordial leads; moreover, this description of the bundle branch block pattern is entirely redundant because its features have been dealt with in detail in the main section on electrocardiography. This section, incidentally, is one of the best from the point of view of correlating information. It is detailed and instructive, but it is tough going with its dearth of illustrations, lengthy paragraphs, the illogical admixture of present with past tenses, and a fairly generous infiltration of ambiguity.

Another minor stricture may be directed at a tendency which is inherent in any many-authored work. It is clearly impossible to correlate entirely the controversial statements of differing authors, but when categorical contradictions appear—as when one author states that the first heart sound is entirely valvular while another states that there are four contributing components—both opinions should at least be supported with evidence. The editor-in-chief appears from his preface to be conscious

of the shortcomings of this first edition.

The authors have endeavored as far as possible to take up the slack between the publication of sound experimental data and their incorporation in a textbook, and indeed they have succeeded in making this text reasonably up-to-date with a helpful

chapter by chapter bibliography including a number of references up to 1952. By and large this book will make a useful addition to the cardiologic bookshelf.

H. J. L. M.

Hormonal and Neurogenic Cardiovascular Disorders. By WILHELM RAAB, M.D., F.A.C.P., Professor of Experimental Medicine and Head of Cardiovascular Research Unit, University of Vermont. 722 pages; 15.5 × 23.5 cm. The Williams & Wilkins Company, Baltimore. 1953. Price, \$15.00.

Dr. Raab has "been concerned about the unnatural gap which separates the dramatically developing field of endocrinology and of its neuroendocrine aspects from the not less fruitful but more conservative advances of clinical cardiology. . . . It is the purpose of this book to convince cardiologists and other physicians that neuroendocrine and endocrine influences play a fundamental and decisive part in the origin and therapeutic amenability of many cardiovascular disorders and that it is necessary to incorporate the established results and concepts of contemporary neuroendocrinology and endocrinology into everyday clinical thinking and acting." The first section deals with the experimental cardiovascular effects of hormones and neurohormones, the second with the cardiovascular features in endocrine and neuroendocrine syndromes, the third with endocrine and neuroendocrine factors in cardiovascular syndromes.

This volume is based upon the author's own work and an exhaustive survey of the literature, as evidenced by a detailed text and by a bibliography of 3,726 references covering 177 pages. The arrangement is good. The summary at the end of each chapter facilitates reading and crystallizes the author's ideas on the subject. There is a wealth of material here, much of which is controversial or conjectural because of the present state of our knowledge of hormonal and neurogenic factors in general. For example, the author states that "the most important physiological fact whose realization is indispensable for the understanding of the occurrence of myocardial hypoxia under the influence of sympathetic stimulation (e.g., during exercise, exposure to cold and emotions), is the excessive and wasteful consumption of oxygen by the heart muscle, elicited by the adrenosympathogenic catecholamines norepinephrine and epinephrine. It leads to myocardial hypoxia if unopposed by oxygen-sparing cholinergic counteraction and it occurs in principle regardless of myocardial work and of coronary flow as a specific chemical process. . . . In some of those numerous cases in which an occluding intramural hemorrhage in a sclerotic plaque of a coronary branch occurs in apparent connection with a sympathicotonic situation (exertion, emotion, surgical operation, etc.), the local mechanical effect of abrupt sympathogenic coronary dilatation may be considered as a possible immediate cause of intramural capillary rupture.'

This is a stimulating book to read. It should be of interest to cardiologists and to endocrinologists.

S. S.

Sectional Radiography of the Chest. By IRVING J. KANE, M.D., Consultant in Chest Diseases, United States Naval Hospital, St. Albans, N. Y., Attending Physician, Chest Diseases, Lincoln Hospital, New York, N. Y., Associate Physician, Diagnostic Roentgenology, Montefiore Hospital, New York, N. Y. 154 pages; 17 × 26 cm. Springer Publishing Company, Inc., New York, N. Y. 1953. Price, \$7.50.

Sectional Radiography of the Chest is mainly an atlas relating the value of body section radiography in the study of chest diseases. However, the first portion of this book is devoted to the principles and methods of this procedure and the various conditions in which it is useful.

REVIEWS 965

While attention is directed to the general applications of sectional radiography, emphasis is placed on the problems of cancer and tuberculosis. Many cases and illustrations are presented to show how this procedure further clarifies some lesions or uncovers others, which are previously unsuspected.

The roentgenogram reproductions are good and the illustration legends are short but adequate. This brief book is an excellent one and one which radiologists and

other physicians interested in chest diseases will find very useful.

J. M. D.

BOOKS RECEIVED

Books received during August are acknowledged in the following section. As far as practicable those of special interest will be selected for review later, but it is not possible to discuss all of them.

- Adrenal Cortex. Transactions of the Fourth Conference, November 12, 13 and 14, 1952, New York, N. Y. Edited by Elaine P. Ralli, M.D., Associate Professor of Medicine, College of Medicine, New York University, New York, N. Y. 165 pages; 24 × 16 cm. 1953. Sponsored by the Josiah Macy, Jr. Foundation, New York, N. Y. Price, \$3.50.
- Aspects of the Psychology of the Tuberculous. A Psychosomatic Medicine Monograph. By Gordon F. Derner, Ph.D., Associate Professor of Psychology and Director of Clinical Psychology Training Program, Adelphi College, Garden City, New York. 119 pages; 24.5 × 15.5 cm. 1953. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York. Price, \$3.50.
- Atomic Medicine. 2nd Ed. Edited by Charles F. Behrens, M.D., Rear Admiral, MC, U. S. Navy, Staff Medical Officer, Eastern Sea Frontier, etc. 632 pages; 23.5 × 15.5 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, \$11.00.
- Die Bewegungsbestrahlung. By Dr. F. Wachsmann and Dr. G. Barth. 192 pages; 24.5 × 17.5 cm. 1953. Georg Thieme Verlag, Stuttgart; Agents for U. S. A.: Grune & Stratton, Inc., New York. Price, Ganzleinen DM 36.-
- A Bibliography of The World Literature on Blood Pressure, 1920–1950. Volume I (Authors and Titles); Volume II (Author Index and Title Index); Volume III (Abstracts). Edited by Ernest K. Koller and Jacob Katz, Bureau of Applied Social Research and School of Public Health, Columbia University. 28 × 21 cm. (paper-bound); pages not numbered. 1952. The Commonwealth of Massachusetts, Boston. Price for the three volumes: \$5.00; sets may be purchased from the Public Document Division, Office of the Secretary of the Commonwealth, Room 116 State House, Boston-33, Massachusetts.
- The Book of Health: A Medical Encyclopedia for Everyone. Compiled and edited by Randolph Lee Clark, Jr., B.S., M.D., M.Sc. (Surgery), Director and Surgeon-in-Chief, The University of Texas, etc.; and Russell W. Cumley, B.A., M.A., Ph.D., Director of Publications, The University of Texas, etc. 834 pages; 26.5 × 18.5 cm. 1953. Elsevier Press, New York. Price, \$10.00.
- Clinical Unipolar Electrocardiography. 2nd Ed. By Bernard S, Lipman, A.B., M.D., Instructor in Medicine, Emory University School of Medicine, etc.; and Edward Massie, A.B., M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Washington University School of Medicine, etc. 309 pages; 22.5 × 14.5 cm. 1953. The Year Book Publishers, Inc., Chicago. Price, \$6.50.

- Extrasystoles and Allied Arrhythmias. By DAVID SCHERF, M.D., F.A.C.P., Associate Professor of Medicine, New York Medical College; and ADOLF SCHOTT, M.D. (Heidelberg), M.R.C.S., Medical Officer in Charge of the Cardiographic Department, Queen Mary's Hospital for the East End, London. 531 pages; 25.5 × 19 cm. 1953. Grune & Stratton, New York. Price. \$15.50.
- Films in the Cardiovascular Diseases: Survey, Analysis, and Conclusions. By David S. Ruhe, M.D., Adolf Nichtenhauser, M.D., Leo L. Leveridge, M.D., Henry J. Weintraub, M.D., and Norton M. Luger, M.D. 128 pages; 23 × 15.5 cm. (paper-bound). 1953. Medical Audio-Visual Institute of the Association of American Medical Colleges, published jointly with The American Heart Association, New York. Price: paper cover, \$1.50; cloth cover, \$2.00.
- Handbook of Differential Diagnosis. By Harold Thomas Hyman, M.D. 716 pages; 20 × 13 cm. 1953. J. B. Lippincott Company, Philadelphia. Price, \$6.75.
- Inhalation Therapy and Resuscitation. Publication Number 156, American Lecture Series. By Meyer Saklad, M.D., Director, Department of Anesthesiology, Rhode Island Hospital, Providence, Rhode Island. (A Monograph in The Bannerstone Division of American Lectures in Anesthesia, edited by John Adriani, M.D., Director, Department of Anesthesia, Charity Hospital, New Orleans, Louisiana.) 343 pages; 24 × 16 cm. 1953. Charles C. Thomas, Publisher, Springfield, Illinois. Price, \$7.50.
- Multiple Myeloma. By I. Snapper, M.D., Director of Medical Education, Cook County Hospital, Chicago, Illinois, etc.; Louis B. Turner, M.D., Research Assistant in Medicine, Mount Sinai Hospital, New York, New York; and Howard L. Moscovitz, M.D., Resident, Second Medical Service, Mount Sinai Hospital, New York, New York. 168 pages; 23.5 × 15.5 cm. 1953. Grune & Stratton, New York. Price, \$6.75.
- Die Nahbestrahlung. By Henri Chaoul and Felix Wachsmann. 225 pages; 24.5 × 17.5 cm. 1953. Georg Thieme Verlag, Stuttgart; Agents for U. S. A.: Grune & Stratton, New York. Price, Ganzleinen DM 39.-
- Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels.

 5th Ed. By The Criteria Committee of the New York Heart Association, Inc., Harold E. B. Pardee, M.D., Chairman; Arthur C. DeGraff, M.D., Clarence E. de la Chapelle, M.D., Cary Eggleston, M.D., Charles E. Kossmann, M.D., Edwin P. Maynard, Jr., M.D., John B. Schwedel, M.D., Harold J. Stewart, M.D., and Irving S. Wright, M.D. 359 pages; 22.5 × 14 cm. 1953. New York Heart Association, Inc., New York. Price, \$4.95.
- Pediatrics. 12th Ed. By L. Emmett Holt, Jr., Professor of Pediatrics, New York University College of Medicine, etc.; and Rustin McIntosh, Carpentier Professor of Pediatrics, Columbia University, etc. 1542 pages; 25.5 × 17.5 cm. 1953. Appleton-Century-Crofts, Inc., New York. Price, \$15.00.
- Peptic Ulcer: Pain Patterns, Diagnosis and Medical Treatment. By Lucian A. Smith, A.B., M.D., M.S. in Medicine, F.A.C.P., Assistant Professor of Medicine, Mayo Foundation, etc.; and Andrew B. Rivers, M.A., M.D., M.S. in Medicine, F.A.C.P., Late Associate Professor of Medicine, Mayo Foundation, etc.; Foreword by George B. Eusterman. 576 pages; 25.5 × 17 cm. 1953. Appleton-Century-Crofts, Inc., New York. Price, \$12.50.

REVIEWS 967

- Roentgen Diagnosis of the Heart and Great Vessels. First American Edition, new enlarged revision. By ERICH ZDANSKY, M.D., Professor of Roentgenology, University of Vienna, etc.; translated by LINN J. BOYD, M.D., F.A.C.P., Professor and Director of Medicine, The New York Medical College, Flower and Fifth Avenue Hospitals. 500 pages; 26 × 18 cm. 1953. Grune & Stratton, New York. Price, \$15.50.
- Stedman's Medical Dictionary of Words Used in Medicine with Their Derivations and Pronunciation Including Dental, Veterinary, Chemical, Botanical, Electrical, Life Insurance and Other Special Terms; Anatomical Tables of Titles in General Use, the Terms Sanctioned by the Basle Anatomical Convention; the New British Anatomical Nomenclature; Pharmaceutical Preparations Official in the U. S. and British Pharmacopoeias or Contained in the National Formulary; Biographical Sketches of the Principal Figures in the History of Medicine. 18th Ed. Edited by Norman Burke Taylor, V.D., M.D., F.R.S.C., F.R.C.S., (Edin.), F.R.C.P. (Can.), M.R.C.S. (Lon.), University of Western Ontario, etc.; in Collaboration with Lieut. Col. Allen Ellsworth Taylor, D.S.O., M.A., Classical Editor. 1605 pages; 25.5 × 17 cm. (limp leather binding). 1953. The Williams & Wilkins Company, Baltimore. Price, \$11.50.
- Stress Incontinence in the Female. By JOHN C. ULLERY, M.D., F.A.C.S., F.I.C.S., Obstetrician and Gynecologist, Pennsylvania Hospital, etc. 149 pages; 26 × 17.5 cm. 1953. Grune & Stratton, New York. Price, \$6.75.
- Die Teleröntgentherapie. By Prof. Dr. W. Teschendorf. 72 pages; 21 × 14.5 cm. (paper-bound). 1953. Georg Thieme Verlag, Stuttgart. Price, Kartoniert DM 8.70.

COLLEGE NEWS NOTES

COMING A.C.P. REGIONAL MEETINGS

Programs for any of these Regional Meetings may be obtained from the Executive Office of the College, 4200 Pine St., Philadelphia 4, Pa., on request about one month in advance of the scheduled date.

ARIZONA, Tucson—October 28

NEW JERSEY, Trenton—November 4

UTAH, Salt Lake City—November 14

PUERTO RICO, San Juan—November 20 and 21

MIDWEST, Milwaukee, Wis.—November 21

NORTH CAROLINA, Chapel Hill—December 3

MICHIGAN, Ann Arbor—December 5

1954

EASTERN PENNSYLVANIA, Philadelphia—January 15
COLORADO, Colorado Springs—January 22 and 23
SOUTHERN CALIFORNIA, Riverside—February 13 and 14
VIRGINIA, Richmond—February 25
KANSAS, Topeka—March 19
SOUTHERN ILLINOIS, Peoria—March—

THE PUERTO RICO REGIONAL MEETING

The Governor, Dr. R. Rodriguez-Molina, and members of the College in Puerto Rico are particularly pleased to be the hosts to the 1953 Regional Meeting of The American College of Physicians. This is the fourth meeting of the College held in Puerto Rico, and not only members and interested physicians from Puerto Rico but Fellows and Associates from Continental United States, Cuba and Latin America are cordially invited. Members of the Puerto Rico Medical Association also are extended a cordial invitation to attend. Dr. Cyrus C. Sturgis, Ann Arbor, Mich., President-Elect of the College, and Mr. Edward R. Loveland, Executive Secretary of the College, will be honored guests.

The program comprises a combination of investigative and clinical work and will be presented by members of the College and by physicians who may soon become members. The work discussed will cover some of today's pressing medical problems as well as some aspects of medicine peculiar to Puerto Rico.

The meeting is under the direction of R. Rodriguez-Molina, M.D., F.A.C.P., A.C.P. Governor for Puerto Rico. Dr. Rodriguez-Molina will gladly furnish advice concerning hotel accommodations; his address, San Patricio Veterans Administration Hospital, P.O. Box 4424, San Juan, P.R.

Program

Friday Evening, November 20, 1953

Puerto Rico Medical Association

Presiding

FEDERICO HERNANDEZ-MORALES, M.D., F.A.C.P.

P.M.

8:30 Multiple Myeloma—Results of Treatment with Urethane.

ELI A. RAMIREZ-RODRIGUEZ, M.D. (Associate) and CALIXTO A. ROMERO, M.D. (by invitation).

8:50 Acute Pancreatitis and Diabetes.

Jose A. de Jesus, M.D. (by invitation); Agustin M. de Andino, M.D. (by invitation); and Francisco Trilla, M.D. (by invitation).

9:10 Bacterial Endocarditis—An Analysis of 52 Proven Cases. Jose M. Torres, M.D. (by invitation).

9:30 Pulmonary Sarcoidosis—Presentation of Four Cases. H. Martinez-Villafane, M.D. (by invitation).

9:50 The Eosinophile Response Following Splenectomy. Federico Hernandez-Morales, M.D., F.A.C.P.

Saturday Afternoon, November 21, 1953

School of Medicine

Presiding

RAFAEL RODRIGUEZ-MOLINA, M.D., F.A.C.P.

P.M.

2:00 The Tropical Research Medical Laboratory of the United States Army. Lt. Col. A. S. Benenson, (MC), USA (by invitation).

2:20 Medical Education in Puerto Rico. E. HAROLD HINMAN, M.D., Ph.D. (by invitation).

2:50 Factors Governing the Diagnosis of Leptospirosis. Rurico S. Diaz-Rivera, M.D., F.A.C.P.

3:10 Sprue—A Review.
R. Rodriguez-Molina, M.D., F.A.C.P.

3:30 Intermission.

3:40 Metabolic Studies in Sprue. AGUSTIN M. DE ANDINO, M.D. (by invitation).

4:00 The Effect of Orally Administered Folinic Acid in Sprue.
RAMON M. SUAREZ, M.D., F.A.C.P.

4:20 Treatment of the Anemias. CYRUS C. STURGIS, M.D., F.A.C.P., President-Elect, The American College of Physicians, Ann Arbor, Mich.

4:50 Greetings from The American College of Physicians. Mr. Edward R. Loveland, Executive Secretary, The American College of Physicians, Philadelphia, Pa.

Social Activities

(For members of the American College of Physicians and their guests)

Saturday, November 21, 1953

P.M.

1:15 Luncheon at the School of Medicine, San Juan.

6:30 Cocktail-Buffet at San Juan Country Club, Santurce.

A.C.P. GROUP INSURANCE PLAN

The Group Health and Accident Insurance Plan adopted by the College is still open to Members, but is limited to those with satisfactory health records. No longer will the Insurance Carrier accept applications without regard to past medical history, but this excludes a very small number of Members. Those who desire may still file applications on a new form procurable from the College Brokers, Claypoole and McCormack, The Association Service Office, 1500 Walnut St., Philadelphia 2, Pa.

Newly elected Members of the College are eligible, regardless of past medical history, for a period of sixty days after election to the College; announcements and appropriate forms are automatically mailed to them.

The Group Health and Accident Plan qualified with the necessary percentage

of subscriptions on April 15, 1953, and was held open to June 30, 1953.

The Professional Liability, or Malpractice, Plan is being taken out by a gradually increasing number of Members. This Plan was not dependent upon a certain percentage of subscribers and thus is still open to all Members. It is the belief of the College Committee on Insurance that the Professional Liability Plan adopted by the College is superior to that of any other carrier on a national basis. Lloyds of London, the carrier, has already appointed attorneys to represent Members of the College in many of the geographical districts of the country, the attorneys being chosen on the advice of key Members of the College in each location. Lloyds also, by contract, has agreed to accept service in any state. With the rapidly changing situation in which an ever increasing number of physicians are sued for malpractice, it is considered generally unsafe to be without protection. A physician may be sued on malpractice charges over a long period of time, because there is no limitation by law on his liability. Cases exist of physicians being sued twenty years after the occurrence of the case under dispute. For full data and application forms, address the Association Service Office, 1500 Walnut St., Philadelphia 2, Pa.

A.C.P. POSTGRADUATE COURSES

The Autumn Postgraduate Bulletin was distributed to all Members of the College and to non-members on the mailing list on August 14, 1953, and several hundred applications for registration have been received at the Executive Offices. Course Number 8, "Ballistocardiography," at the Johns Hopkins Hospital, Baltimore, has already been over-subscribed. Other courses are still open at the time of the preparation of this news item. Those who have not registered are urged to send in their applications to the Executive Offices of the College without further delay.

The matriculation fee for each course is \$30.00 to Members, \$60.00 to nonmembers. All registrations must be made through the Executive Offices of the College, 4200 Pine St., Philadelphia 4, Pa. The schedule of courses for the autumn

of 1953 is as follows:

CARDIOVASCULAR DISEASES: New York University College of Medicine, New York, N. Y.; Charles E. Kossmann, M.D., F.A.C.P., Director; October 12-17.

PHYSIOLOGICAL BASIS OF INTERNAL MEDICINE: Duke University School of Medicine, Durham, N. C.; Eugene A. Stead, Jr., M.D., F.A.C.P., Director; October 12-16.

INTERNAL MEDICINE: University of Chicago School of Medicine, Chicago, Ill.; Wright R. Adams, M.D., F.A.C.P., Director; October 19-23.

CLINICAL NEUROLOGY: Jefferson Medical College of Philadelphia, Philadelphia, Pa.; Bernard J. Alpers, M.D., F.A.C.P., Director; November 2-6.

PRESENT DAY THERAPY AND ITS PHYSIOLOGIC BASIS: University of Utah College of Medicine, Salt Lake City, Utah; Maxwell M. Wintrobe, M.D., F.A.C.P., and Louis S. Goodman, M.D., Co-directors; November 9-13.

 SEMINARS IN INTERNAL MEDICINE: Vanderbilt University School of Medicine, Nashville, Tenn.; Rudolph Kampmeier, M.D., F.A.C.P., and Hugh

J. Morgan, M.D., F.A.C.P., Co-directors; November 16-20.

THE NEWER BIOLOGICAL AND PHYSIOLOGICAL APPROACHES
 TO CLINICAL PROBLEMS: University of Wisconsin Medical School,
 Madison, Wis.; William S. Middleton, M.D., M.A.C.P., and Karver L.
 Puestow, M.D., F.A.C.P., Co-directors; November 16-20.

 BALLISTOCARDIOGRAPHY: Johns Hopkins Hospital, Baltimore, Md.; Benjamin M. Baker, Jr., M.D., F.A.C.P., Director; January 11-13, 1954.

Detailed outlines of all courses may be obtained on request to the Executive Offices. To add greater publicity to one of the new courses on the schedule, to be given at the University of Utah College of Medicine, at Salt Lake City, the detailed outline of the course is herewith published.

COURSE No. 5-PRESENT DAY THERAPY AND ITS PHYSIOLOGICAL BASIS

(November 9-13, 1953)

Department of Medicine, University of Utah College of Medicine, Salt Lake City, Utah

Directors

M. M. WINTROBE, M.D., F.A.C.P. L. S. GOODMAN, M.D.

OFFICERS OF INSTRUCTION

Guest Faculty

J. Burns Amberson, M.D., F.A.C.P., Professor of Medicine, Columbia University College of Physicians and Surgeons; Visiting Physician in Charge, Chest Service, Bellevue Hospital, New York, N. Y.
HARRY EAGLE, M.D., Chief, Experimental Therapeutics, National Microbiological In-

stitute, National Institutes of Health, Bethesda, Md.

ALFRED GILMAN, M.D., Professor of Pharmacology, Columbia University College of Physicians and Surgeons, New York, N. Y.

University of Utah Faculty

W. R. CHRISTENSEN, M.D., Professor of Radiology.

H. W. DAVENPORT, M.D., Professor of Physiology.

L. S. GOODMAN, M.D., Professor of Pharmacology.

M. M. WINTROBE, M.D., F.A.C.P., Professor of Medicine. G. E. CARTWRIGHT, M.D., Associate Professor of Medicine.

H. H. HECHT, M.D., Associate Professor of Medicine.

B. V. JAGER, M.D., Associate Professor of Medicine.

HAROLD BROWN, M.D., Assistant Professor of Medicine.
L. W. JARCHO, M.D., Assistant Professor of Medicine.
JOHN H. McClement, M.D., Assistant Professor of Medicine.
C. M. McNeil, M.D., Assistant Clinical Professor of Pathology.
F. H. Tyler, M.D., Assistant Professor of Medicine.

A. B. FRENCH, M.D., Instructor in Medicine.

W. R. GAYLOR, M.D., Resident Assistant in Medicine.

One of the objectives of the Committee on Postgraduate Courses of the American College of Physicians is to provide a wide selection of institutions and directors. Another objective is to provide courses to serve its members adequately from a geographical standpoint. This course was selected not only for the above reasons but because of the outstanding qualifications of the faculty and interest in the fine work being done at the University of Utah College of Medicine. The University of Utah faculty is being supplemented by three nationally recognized authorities, Dr. J. Burns Amberson and Dr. Alfred Gilman of Columbia University, and Dr. Harry Eagle of the National Institutes of Health.

There will be daily, except Wednesday, roundtable luncheons from 12:00 Noon to 1:30 P.M. with Drs. Amberson, Eagle, Gilman, Cartwright, Goodman, Hecht, Jager, Wintrobe and other Officers of Instruction, for informal discussions.

Hotel Accommodations: Hotel Utah, Salt Lake City 10, Utah; Miss Beverly Lippert, Reservation Manager. Single rooms with bath, \$5.00 to \$11.00; single rooms with detached bath, \$4.00; double rooms with double bed and private bath, \$7.00 to \$13.00; twin-bedded rooms with private bath, \$9.00 to \$13.00; suites, \$13.00 to \$25.00. When writing for reservations identify yourself with the American College of Physicians and this particular course.

TENTATIVE OUTLINE OF COURSE

Monday, November 9

A.M. Session

9:00 Introduction.

9:10- 9:50 Hemolytic Anemias.

Dr. Cartwright and Staff.

9:55-10:15 Thrombocytopenic Purpura. Dr. Cartwright and Staff.

10:20-10:50 Physiologic Basis for Splenectomy.

Dr. Wintrobe.

10:50-11:30 Roundtable on Splenic Disorders.

Drs. Wintrobe, Cartwright and Staff. 12:00- 1:30 Roundtable Luncheon.

P.M. Session

2:00- 3:00 Chemotherapy of Leukemia and Allied Disorders.

Dr. Wintrobe.

3:10-4:30 Roundtable on Hematology.

Drs. Wintrobe, Christensen, Cartwright, McNeil and Staff.

Evening

8:00 Tyndale Lecture.

Aspects of Chemotherapy of Tuberculosis.

Dr. Amberson.

Tuesday, November 10

A.M. Session	
9:00- 9:50	Pathogenic Mechanisms in Bronchogenic Carcinoma. Dr. Amberson.
10:00-10:30	Discussion.
10:30-11:10	Disturbances in Alveolar-capillary Gas Exchange. Dr. McClement.
11:15-11:30	Discussion.
12:00- 1:30	Roundtable Luncheon.
Sym	POSIUM ON PULMONARY EMPHYSEMA AND ITS COMPLICATIONS
P.M. Session	
2:00- 2:20	Diagnosis and Treatment of Pulmonary Emphysema. Dr. McClement.
2:20- 2:40	Cor Pulmonale.
	Dr. Gaylor.
2:40- 3:00	Secondary Polycythemia.
	Dr. Hecht.
3:00- 4:30	Roundtable.
F2	Drs. Amberson, Hecht, McClement and Staff.
Evening	Social.
	Wednesday, November 11
A.M. Session	
9:00-10:30	Staff Rounds.
11:00-11:50	Problems of Unresolved Pneumonia.
	Dr. Amberson.
11:50-12:30	Discussion.
P.M. Session	
	Tour of the Laboratories, University, and City.
Evening	
8:00	Studies in Mode of Action of Antibiotics. Dr. Eagle.
	Thursday, November 12
A.M. Session	
9:00- 9:50	Practical Aspects of Antibiotic Therapy. Dr. Eagle.
10:00-10:50	Synergism and Antagonism of Antibiotics. Dr. Eagle.
11:00-11:30	Discussion.
12:00- 1:30	Roundtable Luncheon.
P.M. Session	
2:00- 2:55	SYMPOSIUM ON DISSEMINATED LUPUS ERYTHEMATOSUS
	Drs. Jager, Cartwright and Staff.
	Detection—L. E. Cells.
	Clinical Manifestations.
	Hematologic Manifestations.
	Symposium on the Therapeutic Uses of ACTH and Cortisone
3:00	Physiologic Basis.
3.00	Dr. Tyler.
	Di. Tylei.

- 3:30-4:30 Roundtable on Therapeutic Indications.
 - Dr. Gilman, Goodman, Wintrobe, Cartwright, Tyler, French and

Evening

8:00 The Acidification of the Urine.
Dr. Gilman.

Friday, November 13

A.M. Session

- 9:00- 9:50 Hypokaliemic Alkalosis.
 - Dr. Gilman.
- 10:00-11:30 Roundtable on Diuretics.
 - Drs. Goodman, Gilman, Davenport, Hecht and Brown.
- 12:00-1:30 Roundtable Luncheon.
- P.M. Session
- 2:00- 4:30 Recent Advances in Drug Therapy.
 - Drs. Goodman, Gilman and Jarcho.

NEW LIPE MEMBER

Dr. William J. Kerr, F.A.C.P., Blue Lake, Calif., is the latest addition to the Life Membership list of the College. Dr. Kerr was for many years Professor of Medicine at the University of California and he was President of the College during 1938-39. He is now retired, residing at Blue Lake.

STANDARDS FOR HOSPITAL ACCREDITATION

The Joint Commission on Accreditation of Hospitals, Edwin L. Crosby, M.D., Director, 660 Rush St., Chicago 11, Ill., now has available for distribution to all interested individuals a booklet delineating the "Standards for Hospital Accreditation." The Joint Commission, administered through the American College of Physicians, the American College of Surgeons, the American Medical Association, the Canadian Medical Association and the American Hospital Association, accepted the former policies and standards of the American College of Surgeons, but certain standards have now been changed and these changes are incorporated in this new publication.

FIFTH TRIENNIAL MEDICAL ALUMNI REUNION, UNIVERSITY OF MICHIGAN

Dean A. C. Furstenberg has announced the Fifth Triennial Medical Alumni Reunion of the Medical School of the University of Michigan at Ann Arbor, October 15-17, 1953. There are two days of scientific sessions and clinics, a Banquet, an evening of convivialities, a Medical School Convocation, and the Michigan-Northwestern football game. Former Staff members of any department of the University Hospital are particularly invited.

JEWISH SANITARIUM AND HOSPITAL FOR CHRONIC DISEASES ESTABLISHES FELLOWSHIPS

The establishment of two Fellowships for clinical and experimental research has been announced by the Trustees of the Jewish Sanitarium and Hospital for Chronic Diseases. The Fellowships, named in the honor of the President of the

Hospital, Mr. Isaac Albert, will be awarded during the fall of 1953. Applicants should write to the Hospital Superintendent, Rutland Rd. and E. 49th St., Brooklyn 3, N. Y.

HEART-IN-INDUSTRY CONFERENCE

Leading cardiologists, industrialists and labor, insurance and government representatives will participate in a conference devoted to the medical and socio-economic problems of the cardiac in American industry at Hotel Statler, New York City, November 20, 1953, under the caption of "Heart-in-Industry" Conference. Dr. John H. Keating, F.A.C.P., President of the New York Heart Association, states that the conference will cover the problem as it relates to the worker, management, insurance, labor unions, and compensation agencies. Dr. Keating has announced the appointment of Dr. Norman Plummer, F.A.C.P., Medical Director of the New York Telephone Company and Chairman of the Cardiovascular Diseases in Industry Committee of the New York Heart Association, as Chairman of the Conference Steering Committee.

Serving with Dr. Plummer will be Dr. Edwin P. Maynard, Jr., F.A.C.P., former President of the New York Heart Association, who will be chairman of the morning meeting; Dr. Irving S. Wright, F.A.C.P., former President of the New York and American Heart Associations, chairman of the luncheon meeting, and Dr. Anthony J. Lanza, F.A.C.P., Chairman of the Department of Industrial Medicine at the Post-Graduate Medical School of New York University, in charge of the afternoon meeting. Other doctors serving will be Dr. John W. Ferree, F.A.C.P., Director of Community Service and Education, American Heart Association; Dr. Delavan Holman, F.A.C.P., Director of the Work Classification Unit, University Hospital, Bellevue-New York University Medical Center; and others.

POSTGRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY

The Annual Postgraduate Institute of The Philadelphia County Medical Society attracts physicians from a large area, especially in the Middle Atlantic States. Customarily, the Institute embraces a four- or five-day program, and is held some time prior to the Annual Session of the American College of Physicians. Future dates for the Institute are: 1954—Philadelphia, March 30-April 2; 1955—Philadelphia, March 29-April 1.

The American Board of Nutrition will hold certifying examinations in Atlantic City, New Jersey, during April 1954. Completed applications of persons wishing to be considered for certification should be in the office of the Secretary not later than February 1, 1954. Application forms may be obtained from the Secretary, Otto A. Bessey, Department of Biochemistry and Nutrition, The University of Texas School of Medicine, Galveston, Texas.

The Fall Meeting of the American College of Cardiology will be held at the Hotel Statler in Cleveland, Ohio on November 6 and 7, 1953. The topic of the meeting will be Congenital Heart Disease. The scientific sessions will be devoted to discussions of various physiologic and clinical findings, methods of diagnosis and surgical treatment. Further information may be obtained from the Secretary, Philip Reichert, M.D., F.A.C.P., 480 Park Ave., New York 22, N. Y.

Dr. Simon Dack, F.A.C.P., President of the New York Society for Circulatory Diseases, announces four scientific sessions scheduled for the year 1953-54. The meetings will be held in room 440 of the New York Academy of Medicine building, 2 East 103 Street, New York, N. Y., on the evenings of October 13 and December 8, 1953, February 9 and April 13, 1954.

Dr. C. S. Keefer Appointed Special Assistant to the Secretary of Health, Education, and Welfare

Dr. Chester Scott Keefer, F.A.C.P., Boston, a Regent of the College and former Governor for Massachusetts, has recently been chosen by President Eisenhower as Special Assistant (Health and Medical Affairs) to the Secretary of Health, Education, and Welfare, Mrs. Oveta Culp Hobby. Dr. Keefer's duties involve reviewing and advising the Secretary on all health and medical programs of the department, including advice on legislation. Director of Evans Memorial Hospital since 1940, Dr. Keefer is a former Chairman of the Committee on Chemotherapeutics of the National Research Council and a former member of the Council on Pharmacy and Chemistry of the American Medical Association.

Dr. Francis James Braceland, F.A.C.P., Hartford, Conn., has recently been appointed by President Eisenhower as a member of the National Advisory Committee to Selective Service, concerning current and future "doctor draft" legislation. Dr. Braceland is Chief Psychiatrist at the Institute of Living at Hartford and is a former President of the American Board of Psychiatry and Neurology.

Dr. Julius Lane Wilson, F.A.C.P., Philadelphia, Director of Clinics and Professor of Medicine in the Henry Phipps Institute for the Study, Treatment and Prevention of Tuberculosis at the University of Pennsylvania, has been selected for the recently made position of Director of Medical Education, Medical Section, National Tuberculosis Association.

Shortly after October 15, Dr. Francis R. Manlove, F.A.C.P., Wilmette, Ill., takes over his duties as Director of the University of Colorado Medical Center, Denver, and Professor and Dean of the Department of Medicine at the University of Colorado School of Medicine. He succeeds Dr. Ward Darley, F.A.C.P., who became President of the University on July 1.

Dr. Turner Z. Cason, F.A.C.P., Jacksonville, and Dr. Warren W. Quillian, F.A.C.P., Coral Gables, received the honorary degree of Doctor of Science at the Centennial Commencement of the University of Florida.

Colonel Charles L. Leedham, MC, F.A.C.P., has been awarded the Legion of Merit for his services as Medical Consultant in the Far East. He has now been transferred to the Surgeon General's Office, U. S. Army, as Chief of the Education and Training Division. Colonel Leedham has been elected Secretary of the Military Medical Section of the American Medical Association.

Dr. Leon Jacobson, F.A.C.P., Chicago, has been appointed by Dr. LeRoy H. Sloan, President of the College, as an advisory member to the Committee on Cancer of the American College of Surgeons. Other national groups, such as the American College of Radiology, the College of American Pathologists, the American Cancer

Society and the National Cancer Institute, have also been invited to appoint advisory members. It is the hope of the Committee on Cancer that the advisory members will sit in on the annual meetings of this Committee and offer advice on matters of cancer control as they pertain to the particular specialties of the advisory members. There are many problems in connection with the care of the cancer patient which involve the advice and services of internists.

Dr. H. R. Litchfield, F.A.C.P., presented two exhibits at the Annual Meeting of the American Pediatric Society in Miami, October 4-9, 1953 and at the International Pediatric Congress in Havana, October 11-14, 1953, entitled: (1) Absorption of Minerals, Especially Calcium and Phosphorus in the Newborn; on Breast Fed Babies and Reconstructed Formulas: a Comparative Study. (2) Terramycin and B₁₂, Their Effect on Growth and Development in the Newborn.

Dr. Mark S. Dougherty, Jr., F.A.C.P., Atlanta, Ga., was appointed Assistant Secretary-Treasurer of the Medical Association of Georgia by the society's council at their meeting held June 14.

At the recent annual meeting of the Missouri Heart Association, Dr. J. Will Fleming, Jr. (Associate), Moberly, was installed as President, and Dr. Earl L. Loyd (Associate), Jefferson City, was elected Vice President.

Dr. Helena Hoelscher (Associate), Cleveland, was elected Assistant Treasurer of the American Medical Women's Association at the annual meeting held recently in New York City.

Dr. Alphonse McMahon, F.A.C.P., St. Louis, President-Elect of the Southern Medical Association, has recently been promoted to Rear Admiral, U. S. Naval Reserve Corps.

Dr. Frank L. Roberts, F.A.C.P., Memphis, has recently been made Associate Dean of the University of Tennessee College of Medicine. President of the Tennessee Health Association, Dr. Roberts joined the University in 1936 and since 1949 has served as Assistant Dean.

Dr. F. Redding Hood, F.A.C.P., Oklahoma City, has recently been elected President of the Oklahoma State Heart Association.

Dr. Sydney Jacobs, F.A.C.P., and Dr. Alan M. Goldman, F.A.C.P., New Orleans, have recently been elected, respectively, President of the Louisiana Trudeau Society and President-Elect of the Louisiana Heart Association.

Dr. J. Burton Glenn, F.A.C.P., Washington, D. C., has been elected President of the recently organized Washington Chapter of the American College of Cardiology. Dr. George W. Calver, F.A.C.P., was chosen Vice President.

Dr. Lawrence Jay Thomas, F.A.C.P., Washington, D. C., was recently elected President of the Diabetes Association of the District of Columbia.

Meeting in Houston recently, the Texas Diabetes Association elected Dr. Raymond L. Gregory, F.A.C.P., Galveston, President, and Dr. George M. Jones,

F.A.C.P., Dallas, and Dr. Lawrence B. Reppert (Associate), San Antonio, Vice Presidents. Dr. Edmond K. Doak, Sr., F.A.C.P., Houston, was named Secretary-Treasurer.

Dr. Ernest H. Falconer, F.A.C.P., San Francisco, Clinical Professor of Medicine at the University of California Medical School, was awarded the degree of Doctor of Laws by his alma mater, McGill University, Montreal, Que., Can., at exercises held early in the summer.

Dr. Cecil O. Patterson, F.A.C.P., Dallas, was elected President of the Texas Society of Gastroenterologists and Proctologists at the recent annual meeting. Dr. Edward J. Lefeber, Sr., F.A.C.P., Galveston, was chosen Second Vice President.

Dr. Joseph F. McVeigh, F.A.C.P., Forth Worth, was installed as President of the Texas Heart Association at the recent annual convention in Houston. At the same meeting, Dr. George R. Herrmann, III, F.A.C.P., Galveston, was named President-Elect and Dr. Daniel D. Warren, F.A.C.P., Waco, was elected Vice President.

At a reorganization meeting of the Association of Pathologists of West Virginia, held recently in Morgantown, the name of the society was changed to the West Virginia Association of Pathologists, and Dr. Milford L. Hobbs, F.A.C.P., Morgantown, was reelected President.

At its recent annual meeting, the Texas Dermatological Association chose Dr. Maurice C. Barnes, F.A.C.P., Waco, as President.

Dr. Walter A. Bloedorn, F.A.C.P., Dean of the George Washington University School of Medicine, Washington, D. C., was one of six faculty members honored by the University Alumni Association at a luncheon held in Washington. Dr. Bloedorn received a scroll in appreciation of the 25 years of service devoted to the School of Medicine.

At the 106th Meeting of the Medical Society of Virginia, being held in Roanoke, October 18-21, Dr. Robert L. King, F.A.C.P., Seattle, Wash., and Dr. Claude E. Forkner, F.A.C.P., New York City, are among the out-of-state participants. Dr. King, who is President of the American Heart Association, is speaking on "Rheumatic Fever and Heart Disease," and is taking part in a Panel Discussion of Cardiac Problems. Dr. Forkner is discussing "Advances in Leukemia" and participating in a Panel Discussion of Treatment of Lymphoma.

Dr. William S. McCann, F.A.C.P., Rochester, N. Y., and Dr. H. Marvin Pollard, F.A.C.P., Ann Arbor. Mich., were among the guest speakers at the 103rd Annual Session of the Medical Society of the State of Pennsylvania, held at Pittsburgh, September 22–25. Dr. McCann, a former Regent of the College, spoke on "Fundamentals of Cardio-respiratory Physiology in Reference to Differential Diagnosis and Treatment of Dyspnea," while Dr. Pollard, College Governor for Michigan, read a paper entitled "Neurogenic and Hormonal Influences on the Gastro-intestinal Tract."

Under the Presidency of Dr. John I. Marker, F.A.C.P., Davenport, Iowa, the Mississippi Valley Medical Society held its 18th Annual Meeting in Springfield, Ill., September 23-25. Participating members of the College and their topics included:

Dr. Alfred Goldman, F.A.C.P., St. Louis, Mo., "Chemotherapy of Tuberculosis"; Dr. Robert M. Kark, F.A.C.P., Chicago, who served as moderator for the Panel on Diabetes; Dr. Alphonse McMahon, F.A.C.P., St. Louis, Mo., who moderated a noon round-table luncheon discussion; Dr. Daniel L. Sexton, F.A.C.P., St. Louis, Mo., who was moderator of the panel on "What's New in Medicine and Surgery"; Dr. Samuel G. Taylor, III, F.A.C.P., Chicago, "Pitfalls in the Treatment of Diabetes"; Dr. Harry B. Weinberg, F.A.C.P., Davenport, Iowa, "What's New in Cardiology"; Dr. Stewart G. Wolf, Jr., F.A.C.P., Oklahoma City, Okla., "Custom vs. Fact in the Treatment of Peptic Ulcer"; Dr. John J. Hammond (Associate), St. Louis, "Coronary Artery Disease, Problems in Differential Diagnosis"; and Dr. Atlee B. Hendricks (Associate), Davenport, Iowa, "Liver Biopsy in the Diagnosis of Hepatomegaly."

Dr. Lowell T. Coggeshall, F.A.C.P., Chicago, and Dr. Myron M. Weaver, F.A.C.P., Vancouver, B. C., Can., were two of the speakers at the First World Conference on Medical Education, held in London, England, August 22–29. The Conference was held under the auspices of the World Medical Association in collaboration with the World Health Organization, The Council for International Organizations of the Medical Sciences and The International Association of Universities, and had as its theme, "Undergraduate Medical Education." Dr. Louis H. Bauer, F.A.C.P., Hempstead, N. Y., former President of the American Medical Association and Secretary General of the World Medical Association, was Secretary of the Organizing Committee for the Conference.

Dr. Nathaniel E. Reich, F.A.C.P., Brooklyn, N. Y., delivered an address entitled "Newer Methods of Treatment of Heart Diseases" at the National Heart Institute in Mexico City, Mexico, on August 18.

Dr. Edward M. Kline, F.A.C.P., Cleveland, Medical Consultant, General Electric Company and member of the Committee on the Cardiac in Industry of the American Heart Association, and Dr. Donald S. Smith, F.A.C.P., Pontiac, Mich., Consulting Cardiologist, Fisher Body Division, were two of the participants in a symposium on "The Heart in Industry." Sponsored by the Golden Clinic-Memorial General Hospital Association, the symposium was held at Elkins, W. Va., September 7-8.

Dr. Samuel Blinder, F.A.C.P., New York City, delivered a paper entitled "Differential Diagnosis of Anterior Chest Pain" before the Second Annual Convention of the American College of Cardiology in Washington, D. C., June 8.

Under the Presidency of Dr. Thomas H. McGavack, F.A.C.P., New York City, the New York Diabetes Association held its First Symposium Day on Diabetes at the Memorial Center for Cancer and Allied Diseases, New York City, on October 8. Dr. J. S. L. Browne, F.A.C.P., Director of the University Clinic, Royal Victoria Hospital, Montreal, Que., Can., was the principal speaker, his topic being "Certain Concepts and Difficulties in Clinical Endocrinology." Dr. Franklin B. Peck, F.A.C.P., Indianapolis, Ind., Director of the Medical Division of Eli Lilly and Company, Indianapolis, and Associate Professor of Medicine at Indiana University School of Medicine, spoke on "Indications for the Use of Various Insulins," with Dr. Benjamin I. Ashe, F.A.C.P., New York City, leading the discussion. Dr. Herman O. Mosenthal, F.A.C.P., New York City, Past President of the American Diabetes Association, discussed "Insulin and Complications of Diabetes—Endogenous and Exogenous Insulin." Dr. Herbert Pollack, F.A.C.P., New York City, presented a paper entitled, "The Nutritional Management of Diabetes," and the discussion was led by Dr. Elaine

P. Ralli, F.A.C.P., New York City. Dr. Martin G. Goldner, F.A.C.P., Brooklyn, N. Y., led the discussion on "The Hyperglycemic Glycogenolytic Factor of Pancreas."

Dr. Walter M. Solomon, F.A.C.P., Cleveland, acted as moderator of a panel discussion on "New Concepts in Treatment of Rheumatic Diseases" which was part of the program of the annual session of the American Society of Physical Medicine and Rehabilitation, which met in Chicago, August 31. Under the Presidency of Dr. Solomon, the American Congress of Physical Medicine and Rehabilitation also held its annual session in Chicago, August 31-September 4. Dr. Howard A. Rusk, F.A.C.P., New York, was one of three who gave a preliminary report on "Results of a Combined Medical and Rehabilitation Program in Tuberculosis." At the latter meeting, 62 papers were presented, ten being read by title.

Dr. Hubert M. Parker, F.A.C.P., Kansas City, Mo., presided over the 31st Annual Fall Clinical Conference of the Kansas City Southwest Clinical Society, held September 28-October 1. Among the guest speakers were Dr. Joseph B. Kirsner, F.A. C.P., Chicago; Dr. Francis D. Murphy, F.A.C.P., Milwaukee, Wis.; Dr. Irvine H. Page, F.A.C.P., Cleveland; and Dr. Stanley P. Reimann, F.A.C.P., Philadelphia. In addition to taking part in two panel discussions and a clinicopathologic conference, Dr. Kirsner gave presentations on "Peptic Ulcer: New Gastric Antisecretory Drugs" and "The Use of Antibiotics in Gastro-intestinal Disease." Dr. Murphy discussed "Acute Cardiac Emergencies" and "Chronic Nephritis and the Nephrotic Syndrome." He also moderated a panel discussion and participated in a clinicopathologic conference. Dr. Page read a paper on "The Present Concepts of Arteriosclerosis" and took part in the color television program and a panel discussion. Dr. Reimann talked on "Relationships to Tumor Pathology of Newer Biological Facts and Concepts," served as moderator for a panel discussion on jaundice and participated in a clinicopathologic conference and another panel discussion.

Many members of the College participated in the 28th Connecticut Clinical Congress of the Connecticut State Medical Society and the Yale University School of Medicine, held in the New Haven Hospital and the Yale School of Medicine, September 16–17. Material presented was in the fields of vascular and blood diseases, psychiatry, pediatrics, general medicine, surgery and other related subjects. Out-of-state speakers included: Dr. Edward F. Bland, F.A.C.P., Dr. Herrman L. Blumgart, F.A.C.P., Dr. Joseph F. Ross, F.A.C.P., Dr. Louis Weinstein, F.A.C.P., all of Boston; Dr. Herbert Chasis, F.A.C.P., Dr. Joseph E. Flynn, F.A.C.P., New York City; Dr. Harold J. Jeghers, F.A.C.P., Washington, D. C.; Dr. William A. Jeffers, F.A.C.P., Philadelphia; and Dr. Irvin Sussman (Associate), Bridgeton, N. J.

Dr. John D. Hartigan (Associate), Omaha, spoke on "Management of Hypertension (New Drugs)" at a meeting of the Nebraska Academy of General Practice held in Kearney, Nebr. Dr. Donald C. Campbell, F.A.C.P., Rochester, Minn., addressed the meeting on "Problems Related to the Anemias."

Dr. E. Charles Kunkle, F.A.C.P., Durham, N. C., Assistant Professor of Medicine at Duke University School of Medicine, and Dr. Vince Moseley, F.A.C.P., Charleston, Professor of Medicine at the Medical College of South Carolina, acted as guest panelists in a discussion of vertigo that was part of the joint meeting of the South Carolina Society of Ophthalmology and Otolaryngology and the North Carolina Eye, Ear, Nose and Throat Society. The meeting was held in Charleston, September 14-16.

Dr. Robert E. Eckardt (Associate), Linden, N. J., has recently been appointed Associate Clinical Professor of Industrial Medicine at the New York University College of Medicine.

Dr. Thomas B. Magath, F.A.C.P., Rochester, Minn., recently became an honorary member of the Medical Faculty of the University of Chile. Professor of Clinical Pathology and Parasitology at the University of Minnesota and Chief of the Division of Clinical Pathology at the Mayo Clinic, Dr. Magath received this honor in recognition of his contribution to the field of parasitology.

As of November 1, Dr. Ewald W. Busse (Associate), Denver, Colo., will become Chairman of the Psychiatric Department of the Duke University School of Medicine, Durham, N. C. Dr. Busse has been Chief of the Division of Psychosomatic Medicine at the Colorado General Hospital, Denver, and has been associated with the Colorado University Medical Center since 1946, where he was in charge of the Mental Hygiene and Child Guidance Clinic and Director of the Electro-encephalograph Laboratory.

Dr. Max Samter (Associate), Oak Park, Ill., has recently been named President-Elect of the Chicago Society of Allergy.

Dr. Hatch W. Cummings, Jr., F.A.C.P., Houston, has recently been elected President of the Texas Academy of Internal Medicine.

Dr. George F. Evans, F.A.C.P., Clarksburg, was elected First Vice President of the West Virginia Medical Association at the annual meeting at White Sulphur Springs, July 23-25.

Dr. Wilburt C. Davison, F.A.C.P., Durham, N. C., Dean and Professor of Pediatrics at Duke University School of Medicine, was recently elected Vice President of the American Pediatric Society.

Dr. Walter L. Bierring, F.A.C.P., President of Alpha Omega Alpha Honor Medical Society, sailed August 7 from Montreal for Europe, with plans to visit Glasgow, Edinburgh, Bristol, Oxford and London, and to attend the International Conference on Medical Education and thereafter the meeting of the World Medical Association at The Hague. Dr. Bierring plans further visits in Brussels, Paris, Heidelberg, Copenhagen and Scandinavia. He worked at the Pasteur Institute in 1894. There are some honorary members of the A.O.A in Great Britain whom Dr. Bierring will visit with the hope of extending through the A.O.A. a closer understanding between our two countries in matters of medical education.

Dr. Edward D. Delamater, F.A.C.P., Philadelphia, Research Professor of Dermatology and Microbiology at the University of Pennsylvania School of Medicine, attended the International Congress on Genetics, which was held August 24-31, at Bellagio on Lake Como, Italy.

Dr. Walter B. Martin, F.A.C.P., Norfolk, Va., President-Elect of the A.M.A., was recently honored at a banquet attended by 175 federal service physicians and a group of physicians from Norfolk, Portsmouth, Richmond, Charlottesville, and Suffolk. Rear Admiral Sterling S. Cook, (MC), U.S.N., F.A.C.P., Medical Director of the Portsmouth Naval Hospital, presided at the dinner; and Dr. J. M. Hutcheson,

F.A.C.P., Richmond, former Vice President, Regent and Governor of the College, was among the speakers who paid tribute to Dr. Martin.

Dr. Joseph T. Freeman, F.A.C.P., Philadelphia, Chairman of the Commission on Geriatrics of the Philadelphia County Medical Society, and Dr. Andrew B. Fuller (Associate), Pittsburgh, have recently been appointed by the Medical Society of the State of Pennsylvania as members of a nine-man Commission on Geriatrics.

Dr. Donald L. Glenn, F.A.C.P., formerly of Urbana, Ill, has recently been appointed Regional Medical Officer for the Eastern Region at Philadelphia of the Pennsylvania Railroad. The appointment was made by Dr. Norbert J. Roberts (Associate), Philadelphia, Medical Director of the Pennsylvania Railroad, who has recently announced an expansion and reorganization of the Medical Department.

Dr. Frank L. Engel (Associate), Durham, N. C., Associate Professor of Medicine at Duke University School of Medicine, has recently been elected a member of the Association of American Physicians.

Dr. Benjamin B. Wells, F.A.C.P., who for several years has been Professor of Medicine and Head of the Department of Medicine at the University of Arkansas School of Medicine, Little Rock, resigned as of September 1, to accept an appointment as Vice President and Senior Editor of the W. B. Saunders Company, medical publishers, in Philadelphia.

Dr. Irving N. Holtzman (Associate), Brooklyn, N. Y., Associate Clinical Professor of Dermatology at New York University-Bellevue Medical Center, has recently been promoted to Attending Dermatologist at the Jewish Hospital, Brooklyn.

Dr. Russell S. Boles, F.A.C.P.. Philadelphia, has recently been appointed Professor of Clinical Medicine at the University of Pennsylvania School of Medicine, and has been named special consultant to the National Cancer Institute, United States Public Health Service, Washington, D. C.

In Connecticut, Dr. C. Louis Fincke, F.A.C.P., Stamford, has been appointed a member of the Connecticut Medical Examining Board to serve the unexpired term of the late Dr. Wilmot C. Townsend, F.A.C.P., Hartford. Dr. W. Bradford Walker, F.A.C.P., Cornwall, has been reappointed to the Public Health Council for a six-year term and Dr. John C. Leonard, F.A.C.P., Hartford, College Governor for Connecticut, has been reappointed to the Commission on the Care and Treatment of the Chronically III, Aged, and Infirm for a four-year term. Dr. Franklin S. DuBois, New Canaan, has been named the physician member of the newly created Council on Mental Health.

Dr. Edward L. Turner, F.A.C.P., Seattle, Wash., assumed his duties on October 1, as Secretary and Administrative Officer of the Council on Medical Education and Hospitals of the American Medical Association. Since 1945 Dr. Turner has served as Dean of the School of Medicine and Chairman of the Division of Health Sciences of the University of Washington.

Dr. George Morris Piersol, M.A.C.P., Philadelphia, and Dr. Nila Kirkpatrick Covalt (Associate), Rocky Hill, Conn., are among the members recently chosen by the American Congress of Physical Medicine and Rehabilitation to serve on a Committee for the Coördination and Integration of Physical Medicine and Rehabilitation in Geriatrics.

Dr. A. James French, F.A.C.P., Ann Arbor, has recently been promoted to Professor of Pathology at the University of Michigan Medical School. At the same institution, Dr. Muriel C. Meyers (Associate), has been advanced to the rank of Associate Professor of Internal Medicine.

Dr. William K. Keller, F.A.C.P., Louisville, was recently awarded an inscribed plaque by the Kentucky Association for Mental Health for his "exceptional contributions in the field of mental health." Dr. Keller is Professor of Psychiatry and Associate in Community Health at the University of Louisville School of Medicine.

Dr. Robert S. Dow, F.A.C.P., Associate Clinical Professor of Medicine at the University of Oregon Medical School, Portland, was recently awarded a Fulbright Research Scholarship which entitles him to study in Italy, where he will continue his research in neurophysiology at the University of Pisa.

Captain Leon D. Carson, (MC), U.S.N., F.A.C.P., Director of the Aviation Medical Acceleration Laboratory at the Naval Air Development Center, Johnsville, Pa., has been appointed Visiting Professor of Aviation Physiology at the University of Pennsylvania School of Medicine. Captain Carson was also reappointed Lecturer in Aviation Physiology at the University's Graduate School of Medicine.

Dr. Howard T. Karsner, F.A.C.P., Washington, D. C., Medical Research Adviser to the Surgeon General of the Navy, was recently named Chairman of the Advisory Medical Board of the Leonard Wood Memorial (the American Leprosy Foundation). Dr. Karsner also was recently appointed a member of the Committee on Medical Research of the American Trudeau Society and was reappointed Chairman of the Committee on Pathology of the Division of Medical Sciences, National Research Council.

Dr. J. J. Kirshner, F.A.C.P., Philadelphia, has recently been appointed Acting Medical Director of Eagleville Sanatorium, Montgomery County, Pa. The two-hundred-bed institution is designed and equipped for the care and treatment of patients suffering from pulmonary tuberculosis. Dr. Kirshner is Associate in Medicine at the Jefferson Medical College and Hospital of Philadelphia, and Chief of the Pulmonary Clinic at the Albert Einstein Medical Center, Southern Division.

Dr. Andrew D. Hart, F.A.C.P., Charlottesville, and Dr. Edward S. Ray, F.A.C.P., Richmond, have recently been appointed by the Honorable John S. Battle, Governor of Virginia, to a committee "to serve in an advisory capacity to the State Board of Health and to make recommendations and suggestions as it deems appropriate" in the attempt to eliminate tuberculosis.

Lt. Col. Weldon J. Walker, F.A.C.P., has been appointed Chief of the Cardiovascular Section at Brooke Army Hospital, Brooke Army Medical Center, San Antonio, Texas. He formerly held the same position at Madigan Army Hospital, Tacoma, Washington.

Dr. Joseph F. Linsman, F.A.C.P., Beverly Hills, California, has been elected president of The Los Angeles Radiological Society for 1953-1954.

OBITUARIES

DR. ALEXANDER GEORGE BARTLETT

Dr. Alexander George Bartlett, F.A.C.P., died in San Francisco on May 28, 1953. His death was due to carcinoma of the colon with extensive metastases. Dr. Bartlett was born in Fresno, California, August 6, 1894.

He attended the University of California, receiving the degree of A.B. in 1920, and his M.D. degree in 1926. During the subsequent year he served as Intern at the University of California Hospital and in 1927 he became connected with the teaching staff of the University of California Medical School, attaining the rank of Assistant Clinical Professor in 1941.

Dr. Bartlett was a member of the San Francisco County Medical Society, the State Medical Society and the A.M.A. He was also a member of the California Academy of Medicine and the American Heart Association. For many years he was interested in arthritis and was an active member of the California Rheumatism Association. He became an Associate in the American College of Physicians in 1948 and a Fellow in 1952.

Dr. Bartlett served in World War I in the Army Ambulance Corps in France and also served with a Mobile Operating Unit. In World War II he was a Lieutenant Colonel in the United States Army and Chief of Medical Service at Camp Roberts, Camp Beal and Fort Ord. He was an able clinician who gave generously of his time and energy to the care of his patients, yet he was greatly interested in teaching, and in spite of great demands on his time from a large clientele, he never neglected his teaching assignments.

Dr. Bartlett will be greatly missed by his teaching associates and students, as he was an enthusiastic and able teacher. His kindly personality and help and his advice aided many patients through trying periods. This constitutes a fine legacy to his patients and friends.

One of Dr. Bartlett's hobbies was early California history, and over the years he built up a fine library of "Californiana," becoming an authoritative student of the subject.

ERNEST H. FALCONER, M.D., F.A.C.P., Acting Governor for Northern California and Nevada

DR. LEROY HEWITT BRIGGS

Dr. LeRoy Hewitt Briggs, F.A.C.P., died in San Francisco, California, June 29, 1953, after several months of chronic illness which caused him to give up his practice in 1952. Dr. Briggs was born in Oakland, California, April 8, 1883.

He attended the University of California, receiving an M.D degree in 1908. During 1908 and 1909 he served an internship in both Providence and Fabiola Hospitals in Oakland. In 1912 Dr. Briggs came to San Francisco as an Assistant in Medicine at the University of California Medical School. Subsequently, through the years he advanced to Clinical Professor of Medicine in 1923, and in 1936 was appointed to the William Watt Kerr Professorship of Clinical Medicine, which position he held up to the time of retirement on account of illness. For many years Dr. Briggs was Physician in Chief of the University of California service at the San Francisco Hospital, devoting much time to supervision of teaching and clinical work.

Dr. Briggs was a past President of the San Francisco County Medical Society, the California Academy of Medicine and the Pacific Interurban Club. In addition to being a Diplomate of the American Board of Internal Medicine, he was a former Member of the Board. In 1947 Dr. Briggs became a Fellow of the American College of Physicians.

With the passing of Dr. Briggs we have lost another of the older type of internist and clinician who, in addition to devoting much time to medical teaching and ward supervision, carry on an active routine of consultation and office practice. His patients, as well as his former students and internes, will greatly miss LeRoy Briggs as he was a father to many of them, always generous in giving help and advice.

ERNEST H. FALCONER, M.D., F.A.C.P., Acting Governor for Northern California and Nevada

DR. WALTER GOLDFARB

Dr. Walter Goldfarb, a Fellow of the American College of Physicians since 1949,

died on June 5, 1953, in New York City.

Dr. Goldfarb was born in New York City on January 21, 1909. He received his B.S. degree from the College of the City of New York in 1930 and his M.D. from Yale University School of Medicine in 1935. He served at various intervals on the staffs of the Kings County Hospital and Bellevue Hospital. During World War II, he served with the U. S. Army Medical Corps, being discharged with the rank of Lieutenant Colonel. At the time of his death, Dr. Goldfarb was Senior Physician of the Veterans Administration Regional Office and Consultant at the Bleuler Guidance Center, Jamaica. He was a Diplomate of the American Board of Psychiatry and Neurology and a member of the American Physiological Society, Sigma Xi, Society of Experimental Biology and Medicine, Association for the Advancement of Psychotherapy, New York Society for Clinical Psychiatry, and the American Psychiatric and American Medical Associations.

It is with real regret that the passing of Dr. Goldfarb is herewith recorded.

IRVING S. WRIGHT, M.D., F.A.C.P.,

Governor for Eastern New York

DR. ALFRED GORDON

Dr. Alfred Gordon, F.A.C.P., Philadelphia, Pa., was born in Paris, France, in 1874, and received his medical degree from the University of Paris in 1899 and from the University of Berne in 1900. He pursued postgraduate work at the University of Munich. He came to the United States very early in his career, and his past appointments include: Associate in Nervous and Mental Diseases, Jefferson Medical College of Philadelphia; Examiner of the Insane, Philadelphia General Hospital; Neurologist, Mount Sinai, Northwestern General and Coatesville (Pa.) Hospitals; Consulting Neurologist, Douglass Memorial, Mercy and Shriners' Hospitals of Philadelphia. During World War I, he was Consultant to the Medical Advisory Board of the Army.

Dr. Gordon was a former president of the Philadelphia Neurological Society and the Philadelphia Medico-Legal Society. He was a member of the College of Physicians of Philadelphia, the Academy of Natural Sciences, American Eugenic Society, Philadelphia County Medical Society, Medical Society of the State of Pennsylvania, American Medical Association, American Association of Pathologists and Bacteriologists, American Neurological Association, American Pediatric Society, American Psychiatric Association and had been a Fellow of the American College of Physicians since 1916, practically a charter member. He retired from active work in 1948. His

death occurred on January 12, 1953.

DR. RAYMOND HUSSEY

Dr. Raymond Hussey, F.A.C.P., scientific director of the Council on Industrial Health of the American Medical Association, died in Chicago on April 15, 1953. His death was caused by a neoplasm of the biliary tract.

Dr. Hussey was born in Greensboro, N. C., December 26, 1883. He was educated in medicine at the University of Maryland, receiving his M.D. degree in 1911. In 1927 he received an honorary M.A. degree from Yale University. On June 14, 1917, he married Edith Woodward who survives him. There are no children.

Early in his medical career he worked as a pathologist in various institutions. From 1915 to 1917 Dr. Hussey was an assistant in pathology at Johns Hopkins University; from 1919 to 1922, an associate in pathology and biophysics, Rockefeller Institute for Medical Research; 1922 to 1924 he was assistant professor of pathology at Cornell University Medical School. At Yale he served first as associate professor, later as professor of pathology from 1924 to 1935. From 1937 to 1945 he served as associate professor of medicine at the University of Maryland. There were many other posts held in clinical medicine and industrial health, all during his active years.

Dr. Hussey was a member of numerous scientific societies. He has written papers covering a wide range of topics in medicine. He was a man of great vision, curiosity, and imagination. These qualities of character and mind he always brought to the work at hand.

As we sum up his life's work, he was a pathologist, clinician, investigator, and always a serious student of the problems of industrial medicine and human relations. His broad vision and imagination gave him deep insight to envision coming events. He always was on the frontiers—his thinking was usually ahead of present day ideas. He was always deeply interested in the human side of things. We have lost a great leader, a great worker, a great thinker in the field of industrial medicine.

HOWARD WAKEFIELD, M.D., F.A.C.P., Governor for Northern Illinois

DR. WARFIELD THEOBALD LONGCOPE

Dr. Warfield Theobald Longcope, F.A.C.P., died April 25, 1953 at Lee. Massachusetts, of pulmonary insufficiency. His 76 years had been filled with accomplishment and honor. Born on March 29, 1877, son of George von S. Longcope and Ruth Theobald Longcope, in Baltimore, Dr. Longcope attended The Johns Hopkins University, receiving his A.B. in 1897, and proceeded to The Johns Hopkins Medical School where he came directly under the influence of its early great teachers, Osler, Welch, Halsted and Kelly and where he was associated with such brilliant colleagues as MacCallum, Abel, Hamman and Thayer. After his degree of M.D. in 1901, Dr. Longcope decided to obtain a fundamental background in pathology and, in Philadelphia, he spent 10 years in this field, advancing from resident pathologist at The Pennsylvania Hospital to Director of the Ayer Clinical Laboratory (1904-1911). In 1909, in addition to his post in pathology, he was made Assistant Professor of Medicine at The University of Pennsylvania and in 1911 he was appointed Associate Professor of Medicine at Columbia University, becoming Bard Professor of the Practice of Medicine at Columbia in 1914, as well as Director of the Medical Services at the Presbyterian Hospital in New York City, which positions he held for seven years. For a few months in 1922 he was Professor of Clinical Medicine at Cornell University Medical College. Dr. Longcope returned to his alma mater in Baltimore in 1922 to be Professor of Medicine in The Johns Hopkins University and Physicianin-Chief of The Johns Hopkins Hospital. This dual assignment he held until his retirement in 1946, when he moved from Baltimore to his summer home on a farm at Lee.

In World War I Dr. Longcope was on active duty in the Medical Corps, in the Surgeon General's Office from August 1917 to July 1918, thence overseas with the American Expeditionary Forces until January 1919. He held the rank of colonel. In World War II Dr. Longcope carried a heavy load in teaching and in patient care, with his staff reduced by the demands of the armed services, and also he made direct

contributions to the war effort by membership on many committees, including the Committee on Medicine of the National Research Council, as well as actively conducting essential research in connection with the Army Chemical Center. These extra duties left their mark on his health and with the return of his assistants, at War's end, he was tired and aged, anxious for retirement, as soon as a suitable successor could be found. Dr. A. M. Harvey, a pupil and former resident of Dr. Longcope, succeeded him in 1946.

In his 45 years from medical graduation to retirement, Dr. Longcope vigorously upheld and advanced the highest standards of the medical profession. He was never content with medicerity and this was reflected in the quality of his teaching, the meticulousness of his investigation, in the students and house staff he trained. First and always with Dr. Longcope it was the welfare of the patient, and adjunct studies were done only if this welfare were not disturbed. He adhered rigidity to that principle. As an idealist, he achieved his goal; he won the lovalty and respect of his

associates and his subordinates.

The contributions Dr. Longcope made to the medical literature were many. His paper in 1914 on syphilitic aortitis remains a classic. He was a recognized authority on nephritis. On Hodgkin's disease, Boeck's sarcoid, atypical pneumonia, hypersensitivity, and the use of BAL in metallic poisoning he wrote extensively. Under Dr. Longcope's guidance, his students and staff did fundamental work on chemotherapy and the antibiotics, recognizing the untoward reactions as well as the favorable features. The importance of his teachings and his investigations led to many honors. From his own alma mater, The Johns Hopkins University, he was given an honorary LL.D. degree in February, 1951. He also held honorary doctorates from St. John's College, the University of Rochester and the University of Paris. In 1934 he was elected a member of the Board of Scientific Directors of the Rockefeller Institute for Medical Research and five years later became its president. He was a member of the Association of American Physicians, American Medical Association, American Association for the Advancement of Science, National Academy of Sciences, Society for Clinical Investigation, American Association of Immunologists, American Society for Pharmacology and Experimental Therapeutics, American Society for Experimental Pathology. Fellow of the American College of Physicians, Harvey Society. Fellow of the Academy of Medicine of New York. The College of Physicians of Philadelphia, Medical and Chirurgical Faculty of Maryland, Fellow of the American Academy of Arts and Sciences, American Clinical and Climatological Association, the Interurban Clinical Club, Honorary Fellow of the Royal Society of Medicine of London, Honorary Member Société des Hópitaux de Paris, Honorary Fellow of the Scandinavian Congress for Internal Medicine. In many of the societies, Dr. Longcope was an officer. In 1948 he was awarded the Kober Medal from the Association of American Physicians for outstanding contributions to medical science.

Professional recognition and distinction did not alter the fundamental character of Dr. Longcope. He was a modest man, somewhat retiring and definitely shy. He was easily embarrassed and this quality often exhibited itself with mannerisms sometimes misunderstood. Above all, he was a sincere man and a loyal friend. His life outside his profession was as full as his vocation. His interests were multiple, in music, in literature, photography, farming, people. His home life was one of simplicity, of generosity and hospitality. Open house for his students and his staff

and Christmas carol singing were characteristic.

Dr. Longcope's death took from the medical profession a man of rare talent and achievement. He lived through a memorable era of medicine and of world history. His loss has been sorely felt.

R. CARMICHAEL TILGHMAN, M.D., F.A.C.P., Governor for Maryland

DR. ANITA MARY MÜHL

Dr. Anita Mary Mühl, F.A.C.P., died December 14, 1952, age 66, of carcinoma. Dr. Mühl was born in Indianapolis, April 19, 1886, was educated in Indianapolis and Germany, received her B.S. (1918) and her M.D. (1920) from Indiana University. She also held the degree of Ph.D. from George Washington University. At one time she taught psychiatry and criminology at the University of Melbourne Faculty of Medicine in Australia. She was author of "A. B. C. of Criminology," a series of thirteen lectures delivered at the University of Melbourne in 1939 and later published for the Austrian Council for Education Research. In 1927 she was appointed Head of the Department of Special Education, a new department created by the California State Board of Education. She had been a Fellow of the American College of Physicians since 1937.

DR. ALBERT A. SCHULTZ

Dr. Albert Andrew Schultz, F.A.C.P., died January 12, 1953, of leukemia in a Des Moines, Iowa, hospital after a lingering illness which had forced his retirement

from practice about a year previously.

Dr. Schultz was born in Tobias, Neb., on May 2, 1887. After attending Lake Forest College for one year, he studied pharmacy and became a Registered Pharmacist in the State of Iowa. He later attended Highland Park College to complete his premedical work and enrolled in Northwestern University Medical School, from which he received his M.D. degree in 1911. He served a rotating internship in Cook County Hospital in 1911–12.

Dr. Schultz entered practice in Fort Dodge, Iowa, and served that community until retiring from practice because of his illness. There he was a member of the staff as well as Electrocardiographer for St. Joseph Mercy Hospital. In addition he was a lecturer at the Hospital Training School for Nurses and was a member of

the staff of the Lutheran Hospital.

During World War I, Dr. Schultz served as Assistant Chief of the Medical Staff of Base Hospital 88. He served terms as President of the Webster County Medical Society and was in 1937 President of the Iowa Clinical Medical Society. He was Chairman of the Section on Internal Medicine of the Iowa State Medical Society in 1933 and 1941 and was a former member of the Pneumonia Control Committee of the State Medical Society. He had been a Fellow of the American College of Physicians since 1940.

Dr. Schultz was a highly respected member of his profession and of his com-

munity, and his death is mourned by his many friends and colleagues.

WILLIS M. FOWLER, M.D., F.A.C.P., Governor for Iowa

DR. DAVID TENNER

Dr. David Tenner died suddenly in Baltimore on May 30, 1953. He was only 48 years of age at the time of his death and though young, he had attained a practice of good proportion and had won the affection of his patients and the respect of his associates.

Dr. Tenner was born in Russia in March 1905 and came to this country in early infancy. He attended the elementary schools in Baltimore and later The University of Maryland, first obtaining his Ph.G. in the School of Pharmacy in 1924 and his M.D in the School of Medicine in 1928. His residency training was at the Mercy Hospital affiliated with The University of Maryland School of Medicine, and from Mercy he went to the Baltimore City Hospitals as resident on the Tuberculosis Service. In 1931 he opened his office for the practice of medicine and in the ensuing 21 years he devoted himself assiduously to private practice, with some teaching on a

part-time basis. He taught Physical Diagnosis at The University of Maryland and was Instructor in Medicine in the Out-Patient Department of The Johns Hopkins University and Hospital. He visited at the Baltimore City Hospitals, the Baltimore Eye, Ear and Throat Hospital, the University Hospital, the West Baltimore General Hospital and was made Associate Chief of Medicine at the Lutheran Hospital in 1946. Dr. Tenner was a Diplomate of the American Board of Internal Medicine, a member of the Baltimore City Medical Society, the American Medical Association and Interstate Postgraduate Medical Assembly. He became a Fellow in the College in 1939.

Dr. Tenner was a quiet, unassuming, energetic and studious physician and his death at an early age removes a well qualified man from the practice of medicine in

Baltimore.

R. CARMICHAEL TILGHMAN, M.D., F.A.C.P., Governor for Maryland

DR. EDWARD J. TURBERT

Dr. Edward J. Turbert, F.A.C.P., died of lung carcinoma on April 3, 1953, at

the New England Deaconess Hospital, Boston, Mass.

Dr. Turbert was born in Southington, Conn., on March 16, 1880. Upon the completion of his preliminary education in Southington, he entered Baltimore Medical College and received his M.D. degree in 1904. He served his internship at St. Francis Hospital, Hartford, Conn. in which city he subsequently established permanent residence, and entered practice.

After many arduous years of general practice, he limited himself to the practice of internal medicine, in which he was active up to the time of his death. He was Visiting Physician to St. Francis Hospital from 1913 to 1952, and Consultant at the Institute of Living, Hartford, and the Manchester Memorial Hospital, Manchester. He was past President of the Hartford Medical Society and past President of the Medical Staff, St. Francis Hospital. He had been a Fellow of the American College of Physicians since 1927.

He is survived by his wife, Mrs. Eleanor Dillon Turbert; a son, Attorney Edward J. Turbert; a daughter, Miss Mary Turbert. He left a host of friends and colleagues who will long cherish his memory. It is with deep regret that we record

his passing.

JOHN C. LEONARD, M.D., F.A.C.P., Governor for Connecticut

DR. JOHN VRENDENBURGH WADSWORTH

Dr. John Vrendenburgh Wadsworth, born September 10, 1894; died suddenly May 6, 1953. He was an Associate of the American College of Physicians since 1928. He graduated from Princeton University in 1916 with a B.S. degree and from the University of Buffalo School of Medicine in 1921. He served as an intern at the Buffalo General Hospital, 1921–1922, and as Resident Physician at the New York Postgraduate Hospital, 1922–24. He was Clinical Assistant at the Buffalo General Hospital from 1928 to 1953, and also Assistant Attending Physician at the Millard Filmore Hospital from 1947 to 1953.

Dr. Wadsworth served as an Instructor in Medicine at the University of Buffalo School of Medicine from 1932 until the time of his death. He was a member of the Buffalo Academy of Medicine, American Medical Association, Nu Sigma Nu and Alpha Omega Alpha fraternities. His chief interest in medicine was gastro-enterol-

ogy. Dr. Wadsworth was highly respected by his colleagues.

EDWARD C. REIFENSTEIN, Sr., M.D., F.A.C.P., Governor for Western New York

DR. ANDREW YEOMANS

Dr. Andrew Yeomans, a Fellow of the College since 1949 and Chief of the Medical Service at the Veterans Administration Hospital, White River Junction, Vt., well known to hundreds of the patients of this hospital and beloved by all who were associated with him, died in Dick Hall's House in Hanover, N. H., on April 17, 1953.

Born in Chicago in 1907, he was graduated from Harvard Medical School in 1935. His extensive postgraduate training included periods of study at the Johns Hopkins Hospital in Baltimore, the Presbyterian Hospital in New York, and the New England Medical Center in Boston.

His four years of war service were spent as the Naval member of the Typhus Commission. He participated in the epoch-making clean-up of typhus fever in Egypt and Italy, the first time in history that a typhus epidemic was brought under control.

After the war he joined the Veterans Administration and was appointed Chief of the Medical Service of the hospital at White River Junction. His work here was the embodiment of the threefold ideal of our medical care program: the highest quality care for our patients, the teaching of young physicians to fill the ever increasing need for well trained doctors in our community, and the quest for new knowledge by carefully planned research on patients under our care.

The quality of care provided under Dr. Yeomans' leadership is well known to us all. His teaching activities included the instruction of not only the resident physicians of this hospital but also the students of the Dartmouth Medical School, where he was appointed Assistant Professor of Clinical Medicine; his principal researches were in the field of the complex mechanisms involved in the regulation of acid-base balance of the body in various obscure diseases. His last publication, in collaboration with Dr. George Stueck, entitled "Clinical-chemical Studies of Acid-base Abnormalities," published in the American Journal of Medicine in August, 1952, attracted widespread attention and resulted in requests for reprints from every state in the Union and from many foreign countries, including some from behind the Iron Curtain.

Fully aware of the relentless progress in his own body of a disease for which there is as yet no known cure, he faced his future with rare courage and serenity of spirit that will provide a lasting inspiration to all who were associated with him. He chose to remain at his work to the last. His constant thought was for the future of this hospital and its patients, the welfare of his residents, and arrangements for continuing his researches in the new laboratory to which he was looking forward. Only a few days before his death, he was in his office completing preparations for a television program for the American College of Physicians on April 15.

In the midst of his busy professional life, Dr. Yeomans found time for active participation in music, which he loved. An accomplished viola player, he found much happiness in the performance of chamber music with his family and friends.

On the evening of April 17, only a few hours after listening to his favorite Haydn string quartettes played near his bedside by his intimate friends, he peacefully joined the eternal company of those who have completed a life devoted to improving the lot of their fellow men.

James H. Townsend, M.D., F.A.C.P., Chief Medical Officer Veterans Administration Center White River Junction, Vermont



Childhood constipation deserves treatment which gently restores normal peristaltic movements; drastic elimination cannot permanently correct the condition and may be harmful to the child.

ROLE OF METAMUCIL* IN ESTABLISHING PROPER BOWEL HABITS IN CHILDREN

Metamucil's bland, demulcent bulk is a physiologic way to manage bowel dysfunction in youngsters.

Metamucil does more than merely clear the constipated bowel. When taken with adequate amounts of water, Metamucil's hydrophilic colloid has a proved corrective effect on the child's misfunctioning intestines. Use of Metamucil early in life assures a natural method of elimination and helps guard against formation of the "laxative habit" in later years.

Mixed with fruit juice, milk or the

child's favorite beverage, Metamucil provides a gentle, corrective stimulation to peristalsis. There is never a "rush"—never a weakening diarrhea with Metamucil.

Metamucil is the highly refined mucilloid of Plantago ovata (50%), a seed of the psyllium group, combined with dextrose (50%) as a dispersing agent. It is accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

SEARLE Research in the Service of Medicine

A NEW CHEMOTHERAPEUTIC MOLECULE TAILORED SPECIFICALLY FOR REFRACTORY URINARY TRACT INFECTIONS O3NOCH = N - N NH H1C - C=0

Discovery of the antimicrobial properties of the nitrofurans provided a novel class of chemotherapeutic agents. These compounds possess specific antibacterial activity with low toxicity for human tissues.

The simplicity and flexibility of this nitrofuran nucleus make possible numerous variations of its chemical and therapeutic characteristics; a remedy may be tailored to fit the disease. Within recent years we have so designed two important antimicrobial nitrofurans for topical use: Furacin brand of nitrofura- O2N OCH=NNHCONH, zone and Furaspor brand of nitrofur-furyl methyl ether.

Now we have succeeded in chemically tailoring a unique molecule, designed specifically for the treatment of bacterial urinary tract infections:



Products of Eaton Research

FURADANTIN

Brand of nitrofurantoin:
N-(5-nitro-2-furfurylidene)-1-aminohydantoin.

for

pyelonephritis cystitis pyelitis

which have proven refractory to other antibacterial agents:

FURADANTIN

provides definite advantages:

clinical effectiveness against most of the bacteria of urinary tract infections, including many strains of Proteus, Aerobacter and Pseudomonas species

low blood level-bactericidal urinary concentration effective in blood, pus and urine-independent of pH limited development of bacterial resistance rapid sterilization of the urine

oral administration

low incidence of nausea—no abdominal pain—no proctitis or pruritus—no crystalluria or hematuria

non-irritating-no cytotoxicity-no inhibition of phagocytosis tailored specifically for urologic use



Scored tablets of 50 & 100 mg. Now available on prescription Write for comprehensive literature

EATONING.

Stop bleeding

from broad capillary bed ...

ue as a hemostat in surgery and in pathologies characterized by hemorrhagic tendencies.*

U. S. Pol. 2,581,850-1952

renose Postoperative

indicated in

Riadds: surrery Tohsillectomy Foislaxis

Ann Woodward Director

How to Retire Progressively

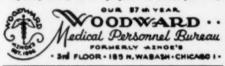


Physicians themselves are responsible for the observation that members of their own profession are among the last to put retirement plans into effect.

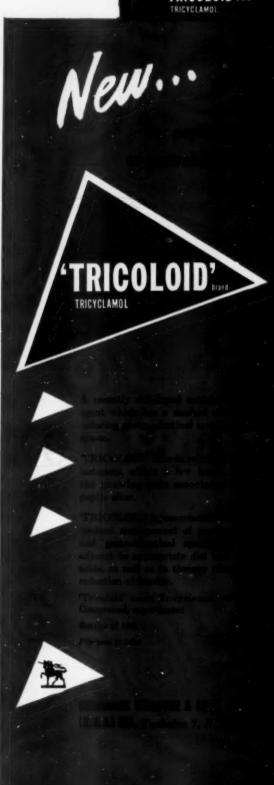
Of course, like anyone else, they make plans. But how, actually, can a man write finis on his role in so many human lives? . . UNLESS he finds someone else who will assume that role conscientiously and with reasonable success. An excellent way to accomplish this end is to delegate some of your responsibilities to an associate whom you have (1) carefully selected; (2) proved competent by gradual induction into your duties.

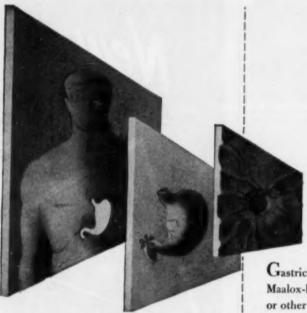
The Woodward Bureau gives swift, systematic service in helping physicians to find associates who measure up. Many fine men in all fields of medicine announce their availability through our channels, and our background of over fifty years in professional placement has alerted us to careful interpretations of individual needs.

Whether your requirements are on a permanent or temporary basis, we are prepared to assist you fully.









maalox

gives ulcer relief

without side effects

Gastric hyperacidity is controlled by Maalox-Rorer without constipation or other side effects commonly encountered with antacids. Relief of pain and epigastric distress is prompt and long-lasting. Available in tablets and liquid form.

Suspension Maalox-Rorer contains the hydroxides of Magnesium and Aluminum in colloidal form. The smooth texture and pleasant flavor make it highly acceptable, even with prolonged use.

Supplied: in 355 cc. (12 fluid ounce) bottles. Also in bottles of 100 tablets. (Éach Maalox tablet is equivalent to 1 fluidram of Suspension Maalox.)

Samples will be sent promptly on request.

WILLIAM H. RORER, INC.

Drexel Bidg., Independence Square Philadelphia 6, Pa.





to prevent attacks in angina pectoris

PATIENT SELECTION—Prophylactic management with Peritrate can be most effective in patients whose attacks come with relative frequency. For instance, Humphreys et al. found that while 78.4 per cent of all patients studied had fewer attacks, "... patients with the greatest number of attacks showed the greatest reduction..."

A RELIABLE CRITERION—Regardless of severity or previous nitroglycerin requirement, Plotz² found that Peritrate decreased the number of attacks in approximately 80 per cent of his patients and "... in all cases the amount of nitroglycerin ... was reduced to half or less..."

rrue angina vs. chest Pain— Peritrate, which seems "specific" for angina pectoris, is virtually ineffective in angina-like chest pains of other etiology: only 5 out of 125 cases of nonanginal chest pain improved compared with 4 out of every 5 verified cases of angina pectoris¹⁻⁸ in

which Peritrate produced

- · fewer attacks of angina pectoris and/or
- reduction in the severity of those attacks which were not prevented.

Since Peritrate must be taken on a daily schedule, patients with occasional mild attacks are best treated with short-acting nitroglycerin.

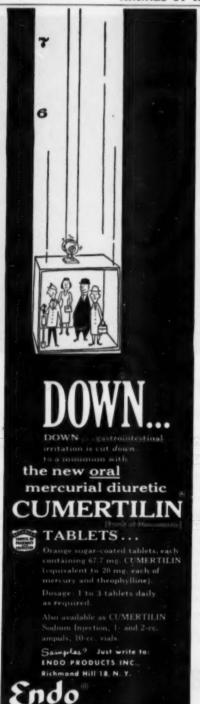
FOR EFFECTIVE PROPHYLACTIC MANAGEMENT-

A long-lasting coronary vasodilator, Peritrate provides prophylactic action for 4 to 5 hours. Administration must be maintained on a continuing daily schedule — usually one tablet 3 or 4 times daily. Some patients require a 2-tablet dose. Peritrate is available in 10 mg. tablets in bottles of 100, 500 and 5000.

BIBLIOGRAPHY: 1. Humpbreys, P., et al.: Angiology 3:1 (Feb.) 1952. 2. Plots, M.: New York State J. Med. 52:2012 (Aug. 15) 1952. 3. Dailbeu-Geoffroy, P.: L'Ouest-Médical, vol. 3 (July) 1950.



WARNER-CHILCOTT Laboratories, NEW YORK



INDEX TO ADVERTISERS

OCTOBER, 1953

Abbott Laboratories 42
American Hospital Supply Corporation 45
Ames Company, Inc 10
Doris Appel Medical Sculptures 14
Doris Appel Medical Sculptures 14 Appleton-Century-Crofts, Inc Second Cover
Ayerst, McKenna & Harrison Limited . 39, 58
Bilhuber-Knoll Corp 13
Borden Company. The
Borden Company, The
Briggs Company, The
Busymatha Wallacome & Co. (11 C A) To-
Burroughs Wellcome & Co. (U.S.A.) Inc. 21, 36, 51
Chicago Dietetic Supply House, Inc 38
Ciba Pharmaceutical Products, Inc 8
Warren E. Collins, Inc
Davies, Rose & Company, Limited
Eaton Laboratories, Inc
Ends Dandorste Inc.
Endo Products, Inc 54
E. Fougera & Company, Inc
Geigy Pharmaceuticals 11
Paul B. Hoeber, Inc
Hoffman-La Roche, Inc Insert facing page 8
Irwin, Neisler & Co 26, 59
Ives-Cameron Company, Inc
LaMotte Chemical Products Co 21
Lea & Febiger 4
Thos. Leeming & Co., Inc 30
Eli Lilly and Company 7
Lloyd Brothers, Inc
Macmillan Company, The 1
S. E. Massengill Company, The 12, 25, 50
Mead Johnson & Company
Medical Protective Company, The 38
Merck & Co., Inc 35
Wm. S. Merrell Company, The 56-57
National Tuberculosis Association 51
Oxford University Press, Inc 2
Pfizer Laboratories, Division, Chas. Pfizer & Co., Inc 6, 16-17. Third Cover
& Co., Inc 6, 16-17. Third Cover
Pitman-Moore Company 28
William H. Rorer, Inc 52
Sanborn Company 24
Schenley Laboratories, Inc 19
Schering Corporation
G. D. Searle & Co
Sharp & Dohme, Division of Merck & Co.,
Inc 46
Silver Hill Foundation, The
Smith, Kline & French Laboratories 29
F. R. Squibb & Sons, Division of Mathie-
son Chemical Corporation 37
U. M. A. Inc 60
Upjohn Company, The 41
U. S. Vitamin Corporation 34
Varick Pharmacal Co., Inc 40
Warner-Chilcott Laboratories, Inc., 9, 53
Williams & Wilkins Company, The 5
Winthrop-Stearns Inc 31
Woodward Medical Personnel Bureau 51
Wyeth Incorporated 18, 43



A THERAPY THAT EMBRACES
IN THEIR NATIVE STATE
THE ENTIRE ALKALOIDS
OF STRAMONIUM

STRAMONIUM PILLS

(DAVIES, ROSE)
O.15 GRAM (APPROX. 2½ GRAINS)

These pills exhibit the powdered dried leaf and flowering top of Datura Stramonium, alkaloidally assayed and standardized, and therefore contain in each pill 0.375 mg. (1/170 grain) of the alkaloids of stramonium.

Sample for clinical test and literature mailed upon request.

DAVIES, ROSE & COMPANY, LIMITED Pharmaceutical Manufacturers Boston 18, Mass., U. S. A.

St 3

Bentyl proves more
effective than atropine
in "Nervous



The Wm. S. Merrell Company . . . Pioneer in Medicine

Indigestion"

McHardy¹ reports that Bentyl is "superior to atropine" for relief of pain due to pylorospasm. He confirms the work of others that Bentyl is free from significant side effects which permits more general use in nervous indigestion.

When you prescribe Bentyl, you prescribe patient comfort. You will rarely hear patients complain about "belladonna backfire" or dry mouth and blurred vision. Use Bentyl for your next nervous indigestion patient. Relief of G.I. spasm is quick, complete and comfortable.

Bentyl

An exclusive development of Merrell Research



New technic of measuring human motility shows a decrease or complete suppression of intestinal pressure waves, depending on dosage of Bentyl.² Bentyl acts by blocking acetylcholine and directly affects the muscle fibers like papaverine.

COMPOSITION: Each Bentyl Capsule or teaspoonful Bentyl Syrup contains 10 mg. Bentyl (dicyclomine) Hydrochloride.

Also Bentyl (10 mg.) with Phenobarbital (15 mg.) Capsules and Syrup, and Bentyl Injection, 10 mg. per cc.

DOSAGE: Prescribe Bentyl, 2 capsules or 2 teaspoonfuls Bentyl Syrup three times daily and at bedtime. Infants and Children, ½ to 1 teaspoonful Syrup 10 to 15 minutes before feeding. Three times daily.

- 1. McHardy and Browne: Sou. M.J. 45:1139, 1952.
- 2. Lorber and Shay: Fed. Proc. 12:90, 1953.

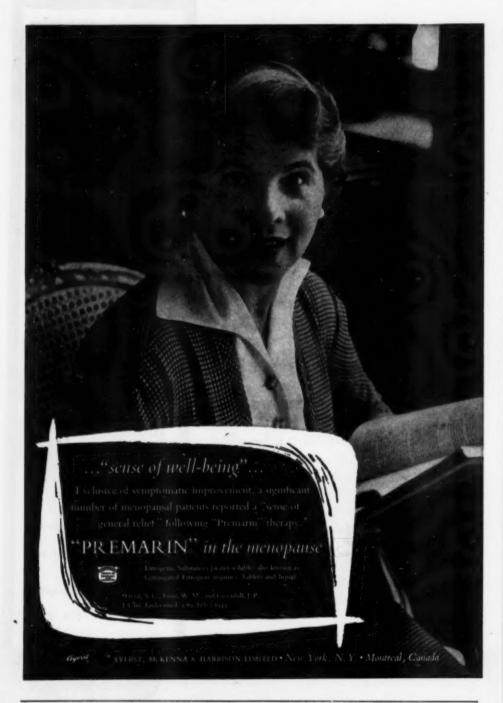
Complete Bentyl bibliography on request.

T.M. 'Bentyl'

for 125 Years

New York
CINCINNATI
St. Thomas, Ontario





Please Mention this Journal when writing to Advertisers

A NEW DRUG...

Announcing

for control of blood pressure

THE TOTAL STATE OF THE PARTY OF

UNITENSEN

Unique Advantages of UNITENSEN

- Of all the known Veratrum alkaloids or Veratrum alkaloid preparations, Unitensen, brand of cryptenamine, is the only one which has a 4:1 ratio between its hypotensive activity and the dosage level which produces the side effect of vomiting.
- Unitensen assures a wide margin between therapeutic and vomiting dose by means of a dual biologic standardization for both emetic propensities and hypotensive action.
- Unitensen has a therapeutic index of 125 highest of all available Veratrum alkaloids tested.
- Unitensen has consistent, predictable and uniform action.

COMPARISON OF UNITENSEN WITH PROTOVERATRINE

Emetic: Therapeutic Ratio	Therapeutic Index
4:1	125
1:1	20
1.2:1	40
1:1	-
1:1	-
	Therapeutic Ratio 4:1 1:1 1:2:1 1:1

Unitensen has shown excellent results in clinical studies in hypertensive crisis, eclampsia, preeclampsia, and preeclampsia with underlying essential hypertension.

Unitensen (Aqueous) is available at present as a parenteral preparation, containing 2 mg. per cc. (260 C.S.R.* Units) of cryptenamine, in 5 cc. multiple dose vials. *Carotid Sinus Reflex

IRWIN, NEISLER & COMPANY . DECATUR, ILLINOIS

Research to Serve Your Practice

THE COLLENS SPHYGMO-OSCILLOMETER

THE OUT

is a blood pressure apparatus and an Oscillometer in one instrument. The OSCILLOMETER is the most important diagnostic aid in Peripheral Vascular diseases for determining the patency of the major vessels in the limbs.





Taking an Oscillometer reading with the COLLENS SPHYGMO-OSCILLOMETER . . .

At your dealer or send for literature

The U.M.A. THERMOCOUPLE

(not illustrated)

is the standard the world over for taking skin temperatures instantaneously and accurately \$125.00

The COLLWIL INTERMITTENT VENOUS OCCLUSION APPARATUS

(not illustrated)

is the proved and accepted simple and automatic therapy whenever impairment of arterial circulation of the limbs occurs \$177.00

U.M.A. Inc.

56 Cooper Square, New York 3, N.Y. - AL. 4-0924

Please Mention this Journal when writing to Advertisers

Taste Toppers . . . that's what physicians and patients elike cell these two for all ages inverte desage forms of



that's what physicians and patients slike cell these two favorite decage forms of Texamycin because of their unsurpassed good taste. They're negalocholic — a treat for patients of all ages, with their pleasant raspbury taste. And they're often the decage forms of first choice for infants, children and adults of all ages.

Terramycin'





Pediatric Drops

Each co. contains 100 mg. of pure crystalline Terramycia. Supplied in 10 cc. bettles with special dropper chilibrated at 25 mg. and 50 mg. May be administered directly or mixed with nonaccidated foods and liquids. Economical 1.0 gram aim often provides the total does required for treatment of infections of average severity in infants.

Supplied: Bottles of 1.0 Cm.

Oral Suspension

Each 5 so, transposatel contains 250 mg. of pure crystalline Terramyols. Effective against gram-positive and gram-cognitive hecteria, including the important coll-servegence group, richettales, certain large viruses and processe.

Supplied: Bottles of 1.5 Cm.



PERMIN LABORATORIUM, Brooklyn 6, N. Y., Division, Chas. Pfiner & Co., Inc.

ANNALS OF INTERNAL MEDICINE

OFFICIAL PERIODICAL OF THE AMERICAN COLLEGE OF PHYSICIANS

EDITOR

MAURICE C. PINCOPPS, M.D., Baltimore

ASSISTANT EDITOR

PAUL W. CLOUGH, M.D., Baltimore

ASSOCIATE EDITORS

DAVID P. BARR, M.D., New York JAMES H. MEANS, M.D., Boston ROBERT A. COOKE, M.D., New York O. H. PERRY PEPPER, M.D., Phila. JAMES J. WARING, M.D., Denver

EXECUTIVE SECRETARY
EDWARD R. LOVELAND, Philadelphia

Editorial Office—University Hospital, Baltimore 1, Maryland Executive Office—4200 Pine Street, Philadelphia 4, Pa. Place of Publication—Prince & Lemon Sts., Lancaster, Pa.

MANUSCRIPTS. All correspondence relating to the publication of pepers and all books and monographs for review should be addressed to the Editor. Bibliographic references are to conform to the following style:

4. Doe, J. E.: What I know about it, J. A. M. A. 96: 2006, 1931.

Six illustrations per article are allowed without cost to the author. Beyond this number the author must pay the actual cost of illustrations.

REPRINTS. For each article published, there will be furnished gratis fifty reprints without covers. An order slip for additional reprints, with a table showing cost, will be sent with galley proof to each contributor. If additional reprints over the first fifty are wanted the order slip must be returned to the printer at the time corrected galley proofs are sent to the Editor.

REVIEWS. Selected monographs and books in the field of internal medicine will be reviewed monthly in the ANNALS. Authors and publishers wishing to submit such material should send it to the Editor. Since it is not possible to review all books submitted, a monthly list of all those received will be published in the review section.

Subscription. This periodical is issued monthly, new volumes beginning with the January and July numbers of each year. Subscription price per annum, net postpaid: \$10.00, United States, Canada, Mexico, Cuba, Canal Zone, Hawaii, Puerto Rico, Philippine Islands, Central and South American Countries, and Spain; \$7.00, in the above countries, to bone fide medical students, interns and residents; \$11.00, other countries. Prices for back numbers furnished upon application. Single numbers, current volume, when available, \$1.25. Checks should be drawn to the order of W. D. Stroun, M.D., Treasurer, and remitted through the Executive Secretary's Office.

BUSINESS CORESPONDENCE. All correspondence relating to business matters, advertising, subscriptions to the Annals, inquiries concerning membership in the American College of Physicians, et cetera, should be addressed to the Executive Secretary. Books and reprints presented to the College Library should be addressed to the Executive Secretary.